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ELECTROCARDIOGRAPHIC FINDINGS IN ANÆMIA

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It has been known for a long time that anæmia is occasionally associated with cardiovascular disturbances, especially with functional cardiac signs and symptoms and with angina pectoris, but there is still a wide diversity of opinion as to the frequency with which this occurs. Detailed electrocardiographic studies have been made less frequently, and so in the present publication such changes are described in cases of pernicious, acute posthæmorrhagic, and chronic hypochromic anæmias, and the conditions in which they occur are discussed.

REVIEW OF PUBLISHED CASES

Herrick and Nuzum (1918) first pointed out that anæmia may be accompanied by angina pectoris, and reported some cases of pernicious anæmia in which anginal pain occurred after effort. Similar cases have been described later by many authors. Coombs (1926) observed typical attacks of angina pectoris in 8 of 36 cases of pernicious anæmia. Lewis (1934) considered angina pectoris as a frequent complication of anæmia, but Willius and Giffin (1927) found only 43 cases with angina pectoris among 1560 cases of pernicious anæmia. Hochrein (1932) and Scherf (1932) stated that anæmia alone causes neither anginal pain nor myocardial damage, and that the occasional disturbances of the coronary circulation in anæmia are always due to organic disease of the coronary arteries. Jagič and Flaum (1935) supposed that there is always a pre-existent latent myocardial damage which becomes manifest in anæmia.

Electrocardiographic changes in anæmia were mentioned by Ussoff (1911) and later by Coombs (1926). But systematic electrocardiographic studies in anæmia have been made only by later authors. Šerf (1929) found in some cases of pernicious anæmia a flat or isoelectric T wave. Turner (1932) observed low voltage in a great number of cases of pernicious anæmia. Elliot (1934) found in one case of anæmia a slight depression of the S-T segment in leads I and II associated with angina pectoris. He concluded that these findings may be the expression of a functional change resulting from anoxæmia of the myocardium. Bloch (1938) found among 88 cases of anæmia electrocardiographic changes in 47 : most frequently flattening of the T wave (in

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87 per cent. of the positive cases), less frequently depression of the S-T segment, and low voltage. De Matteis (1936) studied 32 cases of anæmia ; in 18 of them there were abnormalities, especially changes in the T wave, and it may be of interest that 5 of these 18 were from eighteen to thirty years old, and 10 were younger than fifty years old. Marchal, Soulié, and Roy (1935) reported a case of severe posthæmorrhagic anæmia with low voltage ; immediately after blood transfusion a marked elevation of all waves could be observed. Parade (1933), Bloch (1934), Büchner (1939), Büchner, Weber, and Haager (1935), Aschenbrenner (1934), Herles (1934), Székely (1938), Marchal, Soulié, and Roy (1935), and Dassen and Parodi (1936) have all reported cases in which the electrocardiographic changes disappeared after improvement of the anæmia under treatment.

On the other hand, there are many authors who did not observe any, or only very insignificant, electrocardiographic abnormalities in anæmia, even in those cases in which angina pectoris or intermittent claudication occurred (Reid, 1923 ; Willius and Giffin, 1927 ; Shirley Smith, 1933 ; Pickering and Wayne, 1934 ; Hochrein and Mathes, 1934 ; Misske and Otto, 1937).

PRESENT OBSERVATIONS

Electrocardiographic studies were made in 76 selected cases of anæmia in which clinical examination did not reveal any signs of disturbances of the cardiovascular system, or of any extracardiac affection that may also produce electrocardiographic changes. Cases associated with hyperthyroidism and pulmonary diseases were excluded. The material consisted of 32 cases with pernicious anæmia and 44 with secondary anæmia of the hypochromic type. The erythrocyte count ranged from 850,000 per c.mm. before treatment had begun, to 3,500,000 c.mm., and the value of hæmoglobin from 22 to 75 per cent. We were aware that the majority of the cases of pernicious anæmia were aged patients in whom slight sclerotic involvement of the coronary arteries giving rise to electrocardiographic changes could not be with certainty excluded, in spite of normal clinical findings. But on the other hand, the average age of the patients with electrocardiographic changes was 47·8 years and of those without such changes 44·7 years, which seems to justify the statement that the abnormalities could not be exclusively ascribed to the age and to latent coronary sclerosis. For considering the influence of anæmia on the coronary circulation those cases are of great importance, in which the clinical and electrocardiographic signs suggestive of disturbances of the coronary circulation were only transient and entirely disappeared when the anæmia improved, and those in which the anatomically normal state of the coronary arteries could be verified by post-mortem finding. But owing to the low mortality in anæmia such cases with anatomical verification are very sporadic.

Normal sinus rhythm was present in all cases except in two with auricular and ventricular extrasystoles respectively. The P-R interval was within the usual limits. Lengthening of the intraventricular conduction time was never observed. Left axis deviation was encountered in 10, right axis deviation in

4 cases. In general the following abnormalities were noted : (1) changes of the T wave ; (2) depression of the S-T segment ; and (3) low voltage.

In the series of 32 cases of pernicious anæmia there were electrocardiographic abnormalities in 11 (34 per cent.). The alteration of the T wave was the most frequent abnormality observed. It was seen in 8 cases ; in 2 there was a flat T in leads I and II, in 3 a flat T in leads I, II, and IV, in 2 there was an isoelectric T wave in the three standard leads, and in 1 there was an inverted T in lead I and a flat T in lead II. Depression of the S-T segment was observed in 5 cases and low voltage in 2 cases. Præcordial pain was noted in this group in four cases, but in only one did it have the typical clinical picture, characteristic of angina pectoris. This case had an inverted T wave, especially well marked during the attacks. After improvement of the anæmia, both the anginal pain and the electrocardiographic abnormality entirely disappeared. This case has been followed in our clinic and reported by Prusik and Herles (1934). In the three other cases with præcordial pain the electrocardiogram was normal at rest ; in two of them it was normal even after bodily exercise; in one case there was a slight depression of the S-T segment in leads I and II immediately after exercise.

Among 44 cases of hypochromic anæmia there were electrocardiographic changes in 12 (31 per cent.). In this group also the most frequent abnormality was an alteration of the T wave. It was abnormal in 12 cases ; in 5 it was flat in leads I, II, and III (these changes were associated with low voltage of the initial ventricular complex) ; in 4 it was flat in leads I and II, in 2 in leads I, II, and IV, and in 1 case it was inverted in leads II and III. Depression of the S-T segment in leads I and II was observed in 2, and low voltage in 5 cases. One case with occasional præcordial pain, which had a normal electro-cardiogram at rest, but a slight depression of the S-T segment in leads I and II immediately after exercise, is not included. Low voltage was found exclusively in chronic and severe anæmia. From the five with low voltage in this group, two had myelogenous leucæmia which lasted twelve and sixteen months respectively, two had lymphatic leucæmia which lasted eight and ten months respectively. All these four patients were treated by X-rays before our study. The fifth case with low voltage presented clinically an " idiopathic " septicæmia in which the blood culture was repeatedly negative. Anginal pain occurred only in one case in which the electrocardiogram was normal at rest, but slightly pathological after exercise. The other cases of this group were free of anginal pain.

The frequency of the different electrocardiographic changes found in our cases of anæmia is summarized in Table I.

Except in a few cases, repeated electrocardiograms were taken and correlated with the hæmatological condition. No direct relation was found between the degree of anæmia and the electrocardiographic changes. There were cases in our series in which the red blood cell count and also the hæmoglobin were very low (a million or less and 22 per cent. respectively) and yet the electrocardiogram was normal. On the other hand, there were cases of only slight anæmia with marked changes. Neither the red blood cell count nor the hæmoglobin value were found to be in direct relation to the electrocardiographic changes.

TABLE I

CASES OF ANÆMIA WITH ELECTROCARDIOGRAPHIC CHANGES

Number of Cases and Type of Anæmia	Changes of the T Wave			Depression of the S-T Segment	Low Voltage
	Flat	Iso-electric	Nega-tive		
Pernicious Anæmia ; 11 cases ..	5	2	1	5	2
Hypochromic Anæmia ; 12 cases ..	11	0	1	2	5
Total ; 23 cases	16	2	2	7	7
Percentage	87·3			30·4	30·4

However, in some instances the latter entirely disappeared after improvement of the anæmia under specific treatment. In three cases a pathological T wave became normal, and in three a depressed S-T segment became isoelectric.

One case is reported, of interest both from clinical and electrocardiographic point of view, which may help to explain why severe chronic anæmia does not always produce disturbances of the coronary circulation, and on the contrary why anæmia of moderate degree sometimes results in coronary insufficiency. A man, 34 years old, who had never been ill, complained of slight abdominal pain, symptoms having started suddenly three days before with a profuse hæmatemesis. The heart was normal in size, shape, sounds, rhythm, and rate ; and the blood pressure, 140/90 mm. The lungs were normal. There was no rise of temperature and the sedimentation rate of the erythrocytes was 10 mm. in the first hour and 25 mm. in the second hour. The urine contained no albumin and no sugar. The erythrocyte count was 2,910,000 per c.mm., the hæmoglobin 61 per cent. The leucocyte count was 8,800 per c.mm., of which 65 per cent. were mature polymorphonuclear cells, 5 per cent. stab forms, 23 per cent. lymphocytes, and 7 per cent. monocytes. The first electrocardiogram revealed sinus rhythm, a very slight depression of the S-T segment, a flat T_1, and an inverted T_2 and T_3 (Fig. 1A). Next day the inversion of T_2 and T_3 disappeared, only a flat T wave persisting (Fig. 1B). An electrocardiogram five days later was entirely normal (Fig. 1C). The erythrocyte count the same day was 3,080,000 and later 4,100,000 per c.mm. Electrocardiograms were repeatedly taken and all were normal, including one taken after exercise.

DISCUSSION AND COMMENT

Experimental studies in animals have proved that anæmia may produce ischæmic disturbances of the myocardium, even when the coronary arteries are anatomically intact. Büchner (1932 and 1939) found in rabbits, after an acute massive venesection and artificially provoked exercise, marked changes (depression
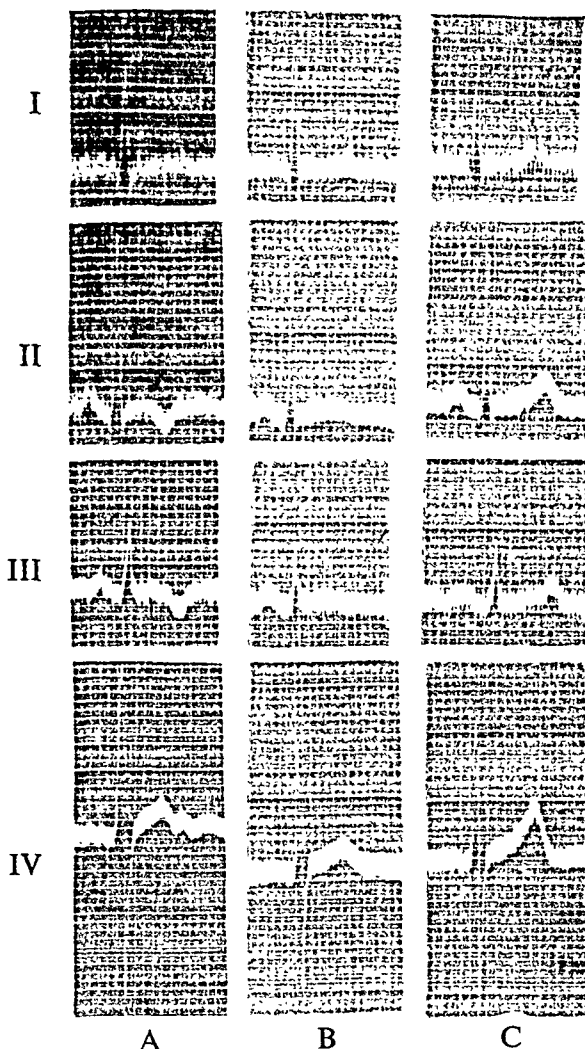
FIG. 1.—(A) Inversion of T_2 and T_3 with hæmoglobin of 60 per cent. (B) T_2 and T_3 flat, one day later, and (C) T_2 and T_3 upright, after six days.

of the S-T segment) which gradually disappeared ; and when these animals were killed after a few days he could demonstrate small areas of recent necrosis in their heart muscle. When they were killed during the first hours after the venesection and exercise, no anatomical changes of the myocardium were found. This author and others (Greene and Gilbert, 1921 ; Rothschild and Kissin, 1932–3 ; and Levy, Barach, and Bruenn, 1938), who experimentally induced anoxæmia and studied the electrocardiogram, found that the specific changes reached their culminating point during the acute oxygen deficiency and disappeared when normal oxygen supply was restored. Ischæmic necrosis of the heart muscle in animals was observed by Büchner only several hours after the condition of supposed acute coronary insufficiency. He concluded that the electrocardiographic changes in these cases are not due to the heart muscle necrosis, but purely to metabolic disturbances of the myocardium resulting from oxygen deficiency, which in anæmia may be caused by diminution of the oxygen-carrying power of the blood.

Laubry and Tzanck (1930) and Marchal *et al.* (1938) pointed out that the pathogenesis of cardiac disturbances seems to be different in acute posthæmorrhagic anæmia and in chronic anæmia. In the first group the anoxæmia of the myocardium is not a decisive factor, but only developes secondarily. The chief and direct cause of the cardiac disturbances may be the insufficiency of the return circulation (insuffisance de la circulation de retour). They could observe that the restoration of the volume of the blood by transfusion or by administration of physiological salt solution was followed by improvement of the clinical signs of cardiac damage and by disappearance of the electrocardiographic abnormalities. On the other hand, in cases of chronic anæmia they attributed a great importance to the anoxæmia of the heart muscle and considered it as the causal factor of cardiac disturbances.

Radnai (1935) made electrocardiographic studies in rabbits after venesection and found approximatively the same progressive changes which were later found by Marchal, Soulié, and Baugé (1938) : accentuation of the T wave, depression of the S-T segment, inversion of the T wave, appearance of a Q wave in lead III, and diminution and enlargement of QRS. Radnai emphasized the identity of these progressive electrocardiographic abnormalities with those found in angina pectoris and considered them anoxæmic in origin.

Experimental findings can only be applied with reserve in the clinical field. Nevertheless there are important clinical facts suggestive of a correlation between anæmia and cardiac disturbances resulting from anoxæmia of the heart muscle ; especially the occasional disappearance of both clinical and electrocardiographic abnormalities after improvement of the anæmia. However, in our cases there was no close parallelism between the degree of anæmia and that of cardiac disturbances. It seems probable that both in acute and chronic anæmia, angina pectoris or electrocardiographic changes are not due merely to the anæmia causing anoxæmia of the heart muscle, but also to another factor. And only the combination of these two factors results in cardiac disturbances. In cases of acute posthæmorrhagic anæmia this additional factor seems to be of reflex vasomotor character. In such instances the coronary volume flow may not be adapted to the acutely altered circulation and acute coronary insufficiency may result with clinical or electrocardiographic manifestations. We believe that our case of acute posthæmorrhagic anæmia, in which the coronary signs in the electrocardiogram entirely disappeared while only a mild improvement of the anæmia was observed, could be explained in this way.

In chronic anæmia the primary myocardial anoxæmia as the direct result of the diminution of the oxygen-carrying power of the blood may play a more decisive role. The experimental results of Marchal *et al* (1938) and of Radnai (1935) may be also in favour of this conception. The small fractional venesections with constant replacement of the volume of the blood by adequate doses of physiological solution may produce, indeed, an important diminution in the hæmoglobin with conservation of the normal blood volume, a condition similar to that in chronic anæmia. And in this experimentally induced anæmia in animals the same electrocardiographic changes were found, *especially*

flattening of the T wave and depression of the S-T segment, and less frequently low voltage, as in certain cases of chronic anæmia in men. But besides the anoxæmic damage of the heart muscle in chronic anæmia, toxic factors must be also taken into consideration as they may affect the myocardium directly. This might be the fact in our chronic cases with low voltage cases in which the electrocardiographic abnormalities were irreversible in spite of temporary improvement of the anæmia.

SUMMARY

Electrocardiographic studies were made in 76 selected cases of anæmia in which there was no clinical evidence of cardiovascular disease. Electrocardiographic abnormalities were found in 23 cases. Most frequently flattening of the T wave occurred ; less frequently depression of the S-T segment and low voltage.

A case is reported of hypochromic anæmia in which inversion of the T wave in leads II and III occurred after a profuse hæmatemesis. These electrocardiographic changes entirely disappeared at an early stage when only a small improvement of the anæmia had been observed.

The pathogenesis of electrocardiographic changes and of cardiac disturbances in general, in acute posthæmorrhagic and in chronic forms of anæmia, is discussed.

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U, THE SIXTH WAVE OF THE ELECTROCARDIOGRAM

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Einthoven (1906) was the first to mention the sixth or U wave of the electro-cardiogram. In 1912 he found it in half the records he examined for this purpose. Lewis and Gilder (1912) first gave statistics of the U wave in healthy people, finding it in 90 per cent., most often in lead II, and of an average height of 0·16 mm. They saw it as a sharp peak immediately after T or as a shallow bending of the whole T-P period. Hering (1913) thought it was aortic and not cardiac in origin.

There are references in various textbooks. Hoffman (1914) described it as " produced by the passive movements of the heart . . . starting after the closure of the semilunar valves . . . belonging to the diastole." Kahn (1914) also thought it important in proving that the end of the electrical activity of the heart is not limited by the T wave. It is mentioned as frequently present (Wiggers, 1923) ; as of unknown meaning (Lewis, 1925) ; as of uncertain origin (Reid, 1928) ; and as of doubtful relationship to ventricular systole (Wenckebach and Winterberg, 1927). In the second edition of his book Pardee (1924) says : " A broad low wave, called U, is sometimes observed following T. It is probably not due to the heart at all, but is caused by the great vessels." There is no reference to it in his third edition (1933) or in the books of Weber (1926) or of Boden (1932).

Hoogewerf (1929), finding it in athletes, thought it might indicate a strong heart ; and Csinady (1930) had a similar impression. Maekawa (1931) studied the electrical events on the muscle strip of the frog's heart and registered the U wave. In human records he separated two types (already mentioned by Lewis and Gilder), of which the short and peak type was held to represent the physiological and the shallow and long type the pathological form. He saw a certain relation between the height of T and of U. Trendelenburg (1934) in various chest leads from normal persons found U always present in one or more leads. Though admittedly a normal wave, " it can become more apparent in cardiac hypertrophy." Gross (1934) agreed that it is a normal event and denied the interdependence of T and U. Hinden (1935) was one of the first to analyse a series of records showing large U waves. In his paper, with figures from the Heart Hospital and the London Hospital, he allowed no distinction in the

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significance of the two forms mentioned by Maekawa, for both were found equally in healthy and in diseased subjects.   Herles (1934) found large U waves in some records taken from dying human hearts, though his two figures are scarcely conclusive.   Holzmann and Wuhrmann (1936) noted increased size of the U wave (as well as of P and T waves) after exertion.   In several cases of Blumberger (1937) it was absent before exertion but appeared after it. Schulz (1938) suggested that a failure of U to appear after exertion might indicate a pathological "deactivation" (inactivationsprozess) in the heart. Székely (1938) found it largest in a chest lead ; there was no direct relation between hypertension and the U wave, but in coronary sclerosis it was less common than in other heart diseases or in healthy people.

Since this investigation was completed, a new and important article on the U wave has appeared, that of Nahum and Hoff (1939).   Investigating the supernormal period of recovery in the mammalian heart, they found that the U wave coincided with it.   While in tachycardia the period fell at the end of T, in bradycardia it appeared closely after T and became visible.   In 75 per cent. of 151 normal human records and in 40 per cent. of 90 pathological records, a U wave of at least 0·25 mm. was found, using lead IV R.   Its maximal height was 1·5 mm. and the average duration 0·20 sec.   In pathological conditions it can be fused with T or can be inverted.   The inverted U may be the only electrocardiographic sign of a damaged heart ; it was seen in coronary, rheumatic, hypertensive, and pulmonary heart disease, and was thought to be due to metabolic changes in the heart muscle, reflected in an altered shape of the after-potential.   The frequent coincidence of extrasystoles with the U wave was considered a further proof that it is the electrical expression of the period of supernormal excitability.

METHOD OF INVESTIGATION

From a large number of electrocardiograms those were selected in which U could be identified in the limb leads.   In about 70 per cent. of normal cardiograms a deflection could be found in one or more leads on the diastolic line, but often so small that neither its dimension nor its duration could be measured. For this reason 0·5 mm. was chosen as the limit in height for this study.   Using this rather strict criterion, the electrocardiograms showing U waves were reduced to about 5 per cent. of 2000 suitable consecutive records, excluding those with auricular fibrillation, flutter, and tachycardia above 110 a minute, in which conditions it proved impossible to identify the U wave.

The patients providing these selected records were studied with regard to the rate of the pulse, blood pressure, clinical diagnosis, and radiological appearances.   The electrocardiogram was examined as to the systolic period and the distribution of the U wave in the different limb leads in health and disease. Investigations were also made on the action of digitalis and quinidine on the U wave.

The physiological U wave changes were watched in healthy men under various conditions.   The limb leads proved unsuitable for studying the slight

changes that might appear under respiratory or effort tests, carotid compression, atropin, or amyl nitrite. Chest leads, especially the IV R standard lead, were used for this purpose. After trying the exploring (proximal) electrode on various sites on the chest wall—left pectoral (Wood and Selzer, 1939), base, and on or external to or internal to the apex—and the indifferent (distal) electrode on the back or on the left leg, it was found that the largest U wave deflections were obtained by lead IV R.

THE U WAVE IN HEALTH

The normal U wave is found at any age from 16 to 75 years, and sex seems to make no difference. At what age the wave appears is undecided. Papers on the electrocardiograms of normal children (Krumbhaar and Jenks, 1917 ; Seham, 1921 ; Lincoln and Nicolson, 1928 ; Bruce, 1931) do not mention it nor contain records showing it.

The height of the normal U wave in limb leads is from 0·10 to 1 mm., and its duration is from 0·16 to 0·24 sec. The shape of the wave—often only a slight hump of the diastolic line—and its variation in size and form in the same record make an exact description difficult. The normal U wave in lead IV R is
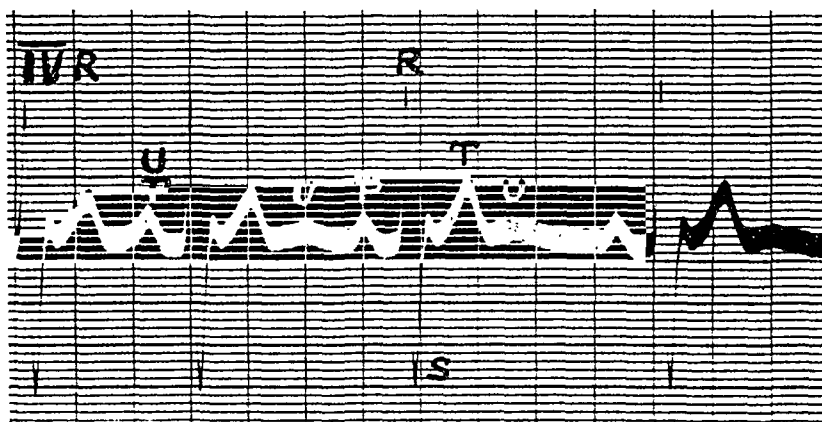
FIG. 1.—Electrocardiogram showing fusion of U and P in tachycardia : with slowing of the heart rate they become dissociated.

upright, 0·5 to 2 mm. in height, with a duration of 0·18 to 0·24 sec., and begins before or closely after the end of T. Its visibility is notably influenced by the heart rate. In tachycardia (over 105–110), when T and the following P are close together, U becomes hidden in P. Indeed, the higher P in tachycardia may be reckoned as partly due to the fusion of P and U (Fig. 1). The first P of this record is 3 mm. high, the others are only 2 mm.

In bradycardia (under 60), the R-T period increases in duration. While with a rate of 80–90 the duration of the whole ventricular complex (from start of Q to the end of T) has an average value of 0·35 sec., with a rate of 52 the R-T period extends to 0·46 sec. (Pardee, 1933). In one of our healthy students, with a bradycardia of 54, the duration of the ventricular complex (Q-T) is generally 0·44 sec. The U wave appears on the record as a hump on the descending

branch of T (Fig. 2, A and C). This deformity of T is recognized as U when the duration of the systolic period (Q-T) decreases, as happens in the slight tachycardia following effort (Fig. 2 B). The maximal duration of the ventricular complex at which U can appear as an independent wave rising from the isoelectric line seems to be 0·40 sec. With a duration of 0·40 sec., U can be
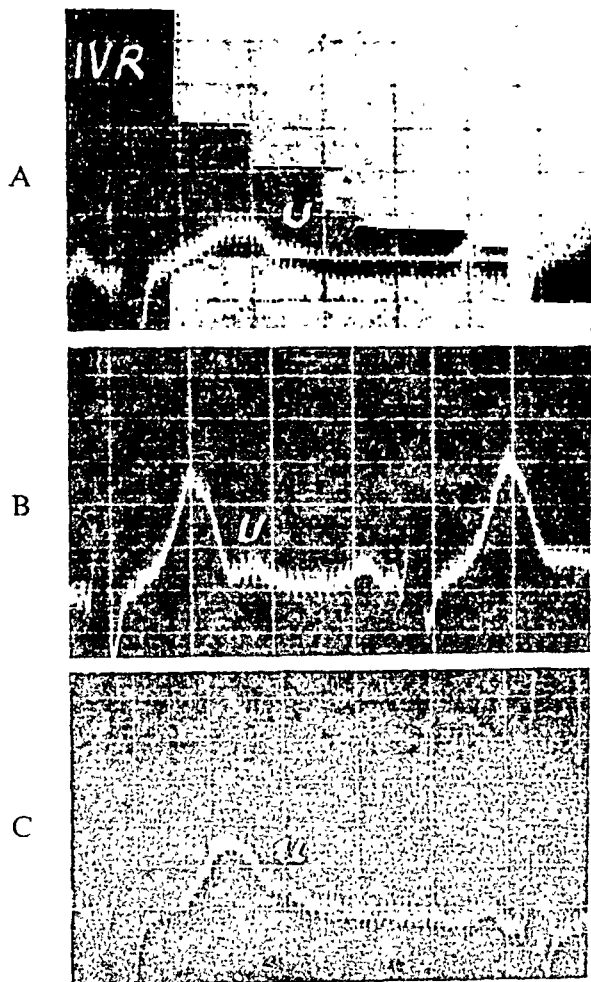
FIG. 2.—(A) Fusion of U and T in bradycardia, 54 a minute : (B) separation of U from T in tachycardia from exertion, 76 a minute : and (C) return to fusion of U with T three minutes later.
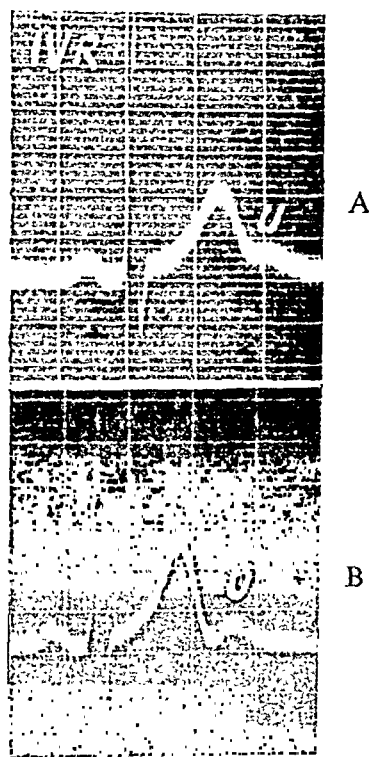
FIG. 3.—Separation of U and T by holding the breath (B), without change in rate.

partially hidden in T yet appear as an independent and larger wave at the end of a forced apnœa (held breath) (Fig. 3 B).

The fusion of U with P in cases of tachycardia or with T when the ventricular complex becomes prolonged prompts the question whether exact time relations between R and U can be established. This can only be answered by studying records in which exact measurements are possible. It is only when U has a sudden onset or is peak-shaped or finishes abruptly on the isoelectric line that R and U time relations can be at all exactly established. Two of the experimental records proved suitable. In one, in which the R–T interval varied

between 0·36 and 0·43 sec. owing to the change in rate with respiration or exercise, the interval R to U peak showed the remarkable stability of 0·42 to 0·44 sec. In the other, the R–U (end) interval of 0·56 sec. remained nearly unchanged when the rate from 52 rose to 72, although the R–T (end) interval decreased from 0·46 to 0·36 sec. Thus the stability of the R–U allows us to consider U as independent of T, to establish certain relations between QRS and U, and to deny any regular time relation between T and U. Respiratory changes of U are seen in sinus arrhythmia ; during inspiration it increases in height and becomes shorter in time, and during expiration it becomes flatter and its duration is prolonged. In such variations one can find in the same record the two types of wave described by Lewis and Gilder (1912) (see Fig. 4). Thus the statement
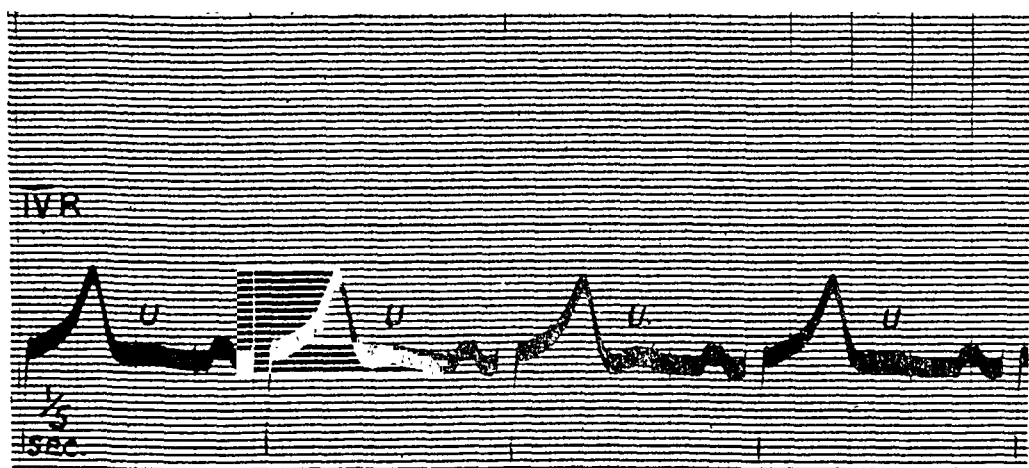
FIG. 4.—Respiratory variations of U. It is sharper and shorter during inspiration.

made by Maekawa (1931) and denied by Hinden (1935), that the short and peaked U is the normal and the large and flat is the pathological U wave, is unfounded.

FURTHER OBSERVATIONS ON HEALTHY MEN

The standard lead IV R was used and the experimental results are given in Table I. Nearly constant experimental results have been obtained on exercise

TABLE I

CHANGES IN THE SIZE OF THE U WAVE UNDER VARIOUS CONDITIONS IN FIVE HEALTHY YOUNG MEN

On Exercise	After 3 minutes	Normal Respiration	Deep Breath	Breath Held	Carotid Compression
+	+ +	R	O	O	—
+	+	O	—	+ +	—
+	+	O	O	+	
+ +	+	O	—	O	O
+ +	+	R	O	+	— —
					+

+ + = increase by more than 0·5 mm.   + = slight increase.
— = decreased.   — — = disappeared.
O = no change.   R = respiratory changes.

(20 knee-bendings), both immediately after and three minutes later. The increase in the size of U on effort does not seem to be due to tachycardia. It remains increased after the tachycardia has ceased and can also be found where there is little or no acceleration after effort. The two cases which showed diminution of U on deep breathing showed the same after carotid compression; in one of them U disappeared, in the other it diminished.

Both methods, especially the latter, produce vagal excitation. The vagal release by atropin (1/50 grain, i.e. 1·3 mg., subcutaneously) had no effect on the U wave in the four observations made. Amyl nitrite was administered in all five cases, but the resultant tachycardia nullified the observations on the U wave. Forced apnœa produced in three of five cases an enlargement of the U wave, most noticeable when the subject could no longer hold his breath.

Increase in height of U is almost always accompanied by increase in the
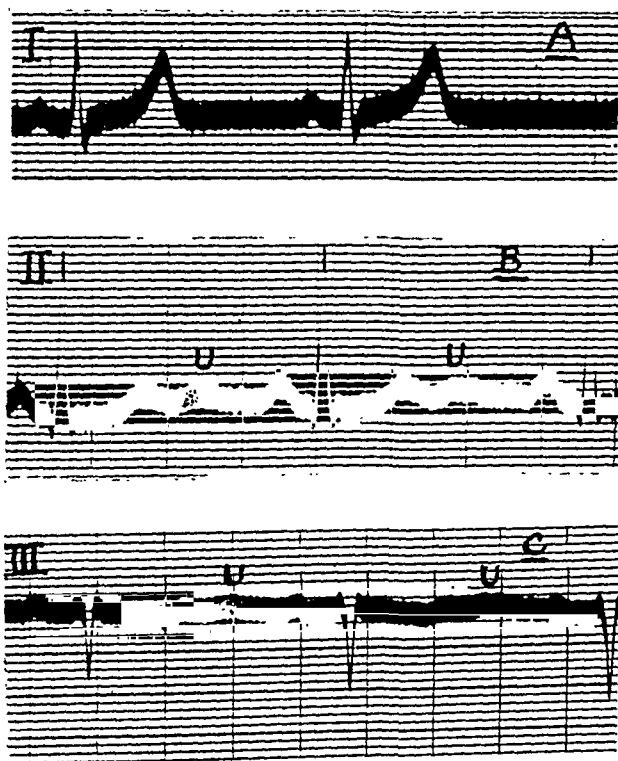
Fig. 5.—Relative independence of size of U and T. Records from three healthy men; (A) U absent with large T; (B) U almost as large as T; (C) U upright after diphasic T.

height of T. The T wave not only enlarges, but changes its shape and becomes rather pointed, especially after effort. Yet in normal conditions big U waves are often observed following small or even inverted T waves (Fig. 5).

THE U WAVE IN DISEASE

A. The Upright U Wave

One hundred consecutive records of patients with heart disease were examined, records in which the U wave was 0·5 mm. high or more in at least one of the three standard limb leads.

1. *Heart Rate.*—This has little importance except that U is scarcely to be identified at rates above 110, as shown by the following figures.

Heart rate per minute	Number of cases in which the U wave was present
40–60	13
60–80	38
80–100	43
above 100	6

2. *Systolic Blood Pressure.*—The frequent incidence (47 per cent.) of hypertension among patients showing a large U is evident from this table.

Systolic Blood Pressure in mm. Hg.	Number of cases in which the U wave was present
90–110	2
110–130	23
130–160	28
160–200	32
over 200	15

3. *Clinical Diagnosis.*—Hypertension in its three groupings is seen to account for no less than 37 per cent., compared with 17 per cent. without heart disease.

Clinical Diagnosis	Number of cases with U wave
No cardiac disease	17
Hypertension without much enlargement	13
Hypertension with cardiac enlargement	19
Hypertension and cardiac failure	5
After Digitalis treatment	11
Extrasystoles	8
Coronary thrombosis and Angina pectoris	11
Thyrotoxicosis	6
Valvular Disease	10

Incidentally, Spang and Korth (1939) found that 20 out of 200 thyrotoxic cases had pronounced U waves in limb leads. Some relationship between the left ventricle and the U wave is suggested by its frequency in conditions affecting the left ventricle, and also by the fact that lead IV R (pertaining especially to the left ventricle) is favourable for its demonstration. It was easy to find among young and athletic students many with large U waves. This bears on the statements of Csinady (1930) and Hoogewerf (1929). Bramwell and Ellis's (1931) paper contains records of two long-distance runners with prominent U waves. Congenital heart disease seldom shows records with large U waves, even where all the ventricular deflections are greatly enlarged in the right axis deviation.

Heart Failure.—Besides the five cases of hypertensive failure quoted, fifty other cases of failure with normal rhythm were examined and in three only was U present before digitalis therapy. In four others in this extra series it appeared only after digitalis. In general, U tends to be less frequent and smaller in heart failure (certainly left) than in its absence.

Digitalis.—In 11 cases U was seen only after digitalis treatment, but in 6 of these there had been tachycardia, fibrillation, or flutter, which would have

prevented its recognition even if present. The remaining 5 show that it may be accentuated or even produced by digitalis (Fig. 6). No effect on the U wave was noticed even after prolonged administration of quinidine.
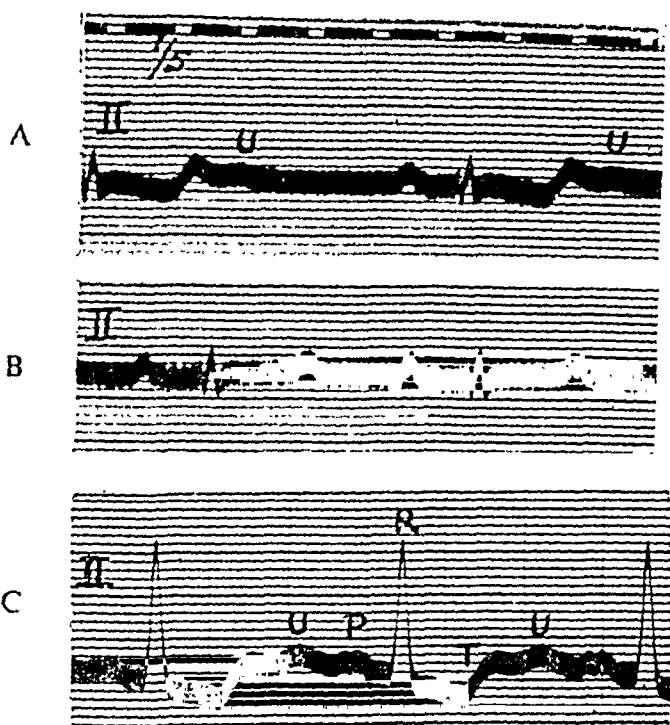
FIG. 6.—Digitalis effects. (A) The U wave is well seen after full doses of digitalis ; and (B) absent four weeks after it was stopped : (C) Very large U waves following prolonged digitalis administration.

4. X-ray Findings.

X-ray Findings	Number of cases with U Wave
Normal heart	45
Slight if any enlargement	12
Slight enlargement of left ventricle	16
Moderate enlargement of left ventricle	17
Enlargement of right and left ventricle	6
Characteristic of mitral stenosis	4

5. *Electrocardiographic Findings.*—In half the hundred records showing a large U the electrocardiogram was normal. When abnormal, the change usually concerned the T waves. In 32 with flattened or inverted T, U was upright—a fact which stresses their independence in disease as already described in health.

Electrocardiogram	Number of cases with U Wave Upright	Inverted
Normal	50	0
Left axis deviation	6	0
Right axis deviation	1	0
T_1, T_2 changes from Hypertension . . .	14	4
T_1, T_2 changes from Coronary disease . . .	12	2
T_2, T_3 changes from Coronary disease . . .	5	2
R–T depression (digitalis)	3	0
A–V dissociation	1	0

The systolic period R–T showed, using Pardee's table (Pardee, 1933), in 78 per cent. a normal value, in 14 per cent. slight prolongation, and in 8 per cent. distinct prolongation. Contrary to the opinion of Einthoven (1912) and Maekawa (1931), therefore, no relationship was found between the presence of U and the lengthening of systole.

6. *Distribution of Upright U in Leads I, II, and III.*—U appears most often in lead II, and it was present in this lead in 87 per cent. While U in lead II was found equally in normal and in pathological records, the isolated appearance of U in leads I or III was, with one exception, in pathological records.

	Cases	U_1	U_2	$U_{1,2}$	$U_{2,3}$
Normal electrocardiogram . . .	55	1	44	8†	2
Left axis deviation	6	—	4	1†	1
Right axis deviation	2	—	—	2	—
T_1, T_2 changes in hypertension . .	14	1	10*	2	1
T_1, T_2 changes in coronary disease .	13	4	9*	—	—
T_2, T_3 changes in coronary disease .	5	2	3*	—	—
R–T depression (digitalis) . . .	5	1	3*	1	—
	100	9	73	14	4

* Including in each case one with U_3 only.
† Including in each case one with U_1, U_2, and U_3.

B. The Inverted U Wave

In 8 per cent. of the series an inverted U wave was seen in the limb leads, and it could always be confirmed in lead IV R. The patients concerned had coronary thrombosis (5 cases, 3 with hypertension) or hypertension alone (3 cases). With one exception T changes were always present. Three cases of coronary thrombosis were of the T_1 type, and two cases of the T_3 type (Fig. 7).
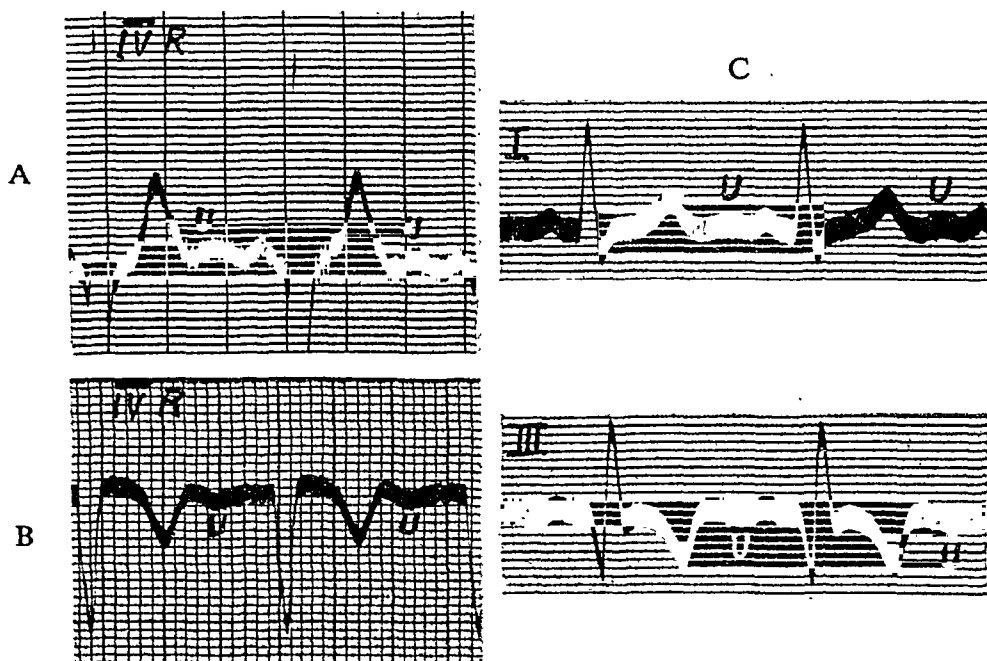

FIG. 7.—(A) Before, and (B) three weeks after coronary thrombosis, to show inversion of the U wave. T_1 was also inverted (anterior infarct). U is identified by measurement from R or from S; (C) three weeks after posterior coronary thrombosis in another case.

A transition stage from upright to inverted U is shown in Fig. 8, where U is diphasic in IV R.
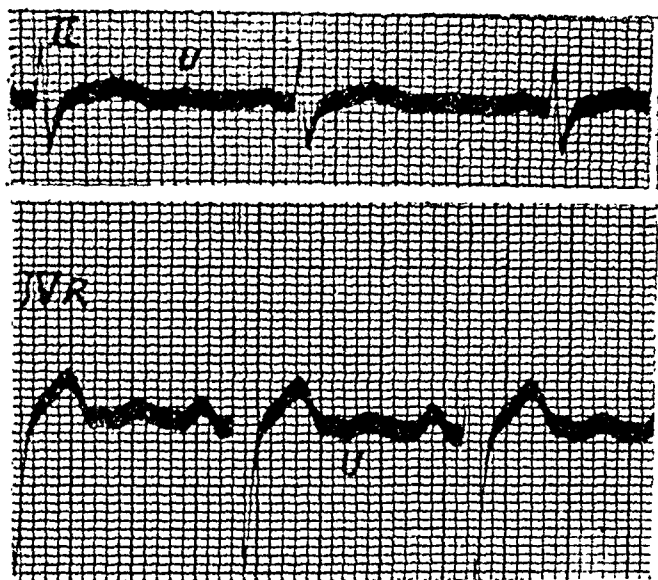
FIG. 8.—Diphasic U in lead IV R with upright U in lead II.

Inversion of the U has never been seen by me nor has it ever been reported in a normal electrocardiogram, so must be considered pathological. This new sign, not previously described except by Nahum and Hoff (1939), may become of some clinical value. It may prove the only pathological sign (Fig. 9).

With Extrasystoles and Bundle Branch Block

If ventricular extrasystoles are accompanied by a U wave, this is often upright ; but where the S component is inverted, U may be inverted. U is seldom seen in pathological bundle branch block ; and among 60 such cases it was only seen in four limb lead records. This rarity can scarcely be due to the long duration of the ventricular complex, for this rarely exceeds 0·40 sec., a period which would permit its recognition. In the common type of bundle branch block the U wave is generally inverted in lead I and upright in lead III, following the direction of S (Fig. 10). Comparing records from two patients, the one without failure showed U only in left pectoral-R (Wood and Selzer, 1939), but the other with failure, using the same lead, did not. U was never seen in bundle branch block with failure.

In bundle branch block with a short P–R interval, the so-called Wolff, Parkinson, and White syndrome (1930), there may be a reversion of the short P–R wide QRS complexes to normal complexes. The U wave, when absent in the former, may be evident in the latter (Tung, 1936 ; Fig. 8 in Wolff, Parkinson, and White, 1930).

RECOGNITION OF THE U WAVE

This may be difficult in simple bradycardia or tachycardia owing to its fusion with T or P respectively (Fig. 1, 2, & 3). When in tachycardia the T–P

FIG. 9.—Inverted U as an isolated electrocardiographic sign in lead IV R. The R–U distance in leads III and IV R is the same ; from a man with hypertension and angina of effort.

FIG. 10.—Left bundle branch block ; inversion of U in lead I.

distance has the same length as a large U wave, the curve may resemble that of auricular flutter. A premature auricular beat with blocked ventricular complex may look like a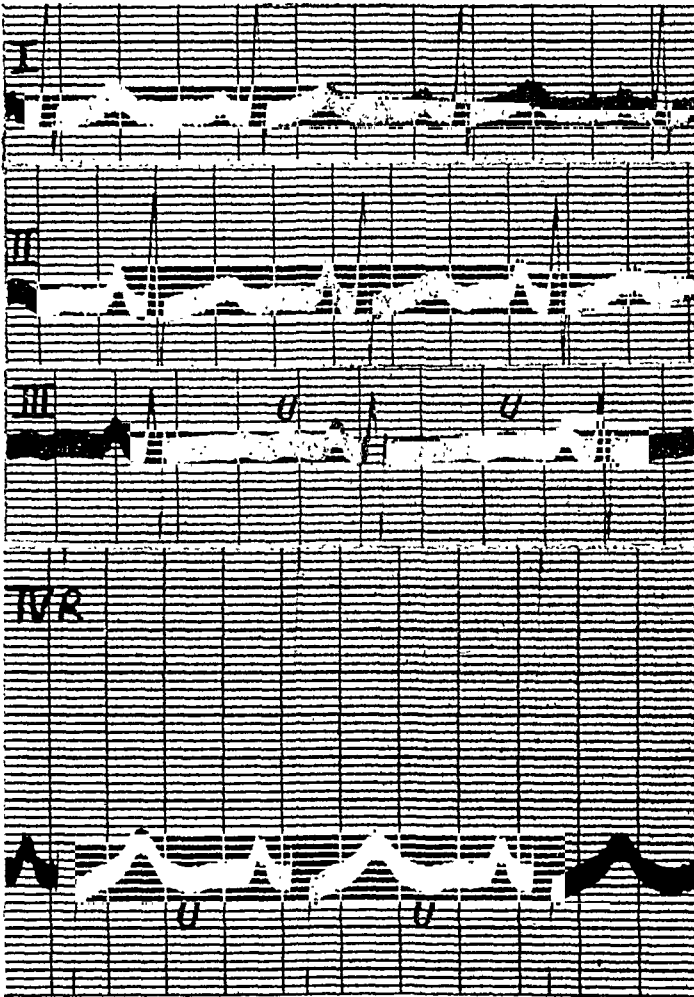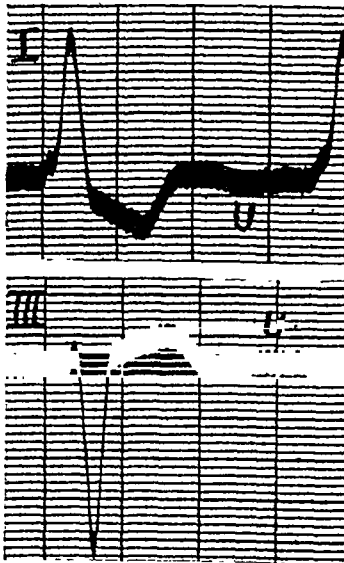 U wave, but there is a compensatory pause to be explained. The greatest difficulties, however, arise in the rare cases of bifid T wave. Such a wave may be followed by U, so that there are three upright deflections between
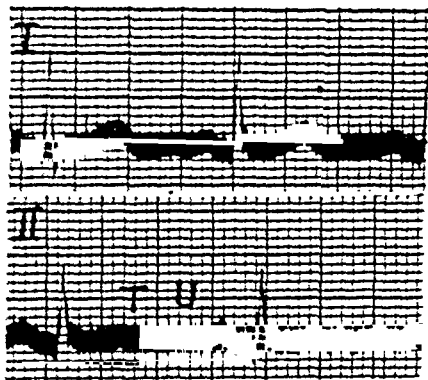
FIG. 11.—Presence of bifid T along with U. The R–T distance, measured in lead I, covers T but not U in lead II.

R and P (Fig. 11). In this record, the R–T (end) distance in lead I, measured on lead II, shows that the second deflection after R must be included as part of T.

INTERPRETATION OF THE U WAVE

The several hypotheses advanced to explain the U wave may first be divided into the extracardiac and the cardiac.

1. *Extracardiac hypotheses.*—Hering (1913) viewed the U wave as the electrical expression of the aortic contraction. Lewis (1915) disagreed, finding its occurrence so long after the carotid pulse incompatible with an aortic source. Trendelenburg (1934), knowing that an electric current may be generated at the end of systole by a rapid blood flow, thought that this might account for it. All subsequent evidence has been against this view, which also may be dismissed. Similarly there is no evidence that the swing of the heart during diastole could originate such an electrical disturbance as the U wave manifests.

2. *Cardiac hypotheses.*—The almost constant time relation with QRS, a certain but limited correspondence with the size and direction of T, and the influence on U of several factors that also affect the heart, all go to prove that the U wave is part of the electrical expression of cardiac activity or an immediate consequence of it. Its position on the borderline between systole and diastole raises the important question, to which of these does it belong ? According to Einthoven (1912) and Maekawa (1931), the main part of the heart muscle is already in a state of relaxation when U appears, but a few muscle fibres are still in contraction: it would then be the expression of a " dying away of the contraction," a systolic product though appearing early during diastole. On the other hand, Lewis and Gilder (1912), Trendelenburg (1934), and Lewis (1937) regard U as belonging to diastole. Its position in relation to the polygraphic (venous

pulse) tracing should enable us to place it correctly in regard to the cardiac cycle. With a normal heart rate, it begins coincidently with the peak of the " v " wave or somewhat later, i.e., after the opening of the A–V valves (Fig. 30, Lewis, 1925), and not with the ascending portion of " v " as presented in the diagram by Lewis (1925) (his Fig. 24). Not only by reference to his Fig. 30, but by measurement of our similar figure (Fig. 12) the coincidence of U with the peak
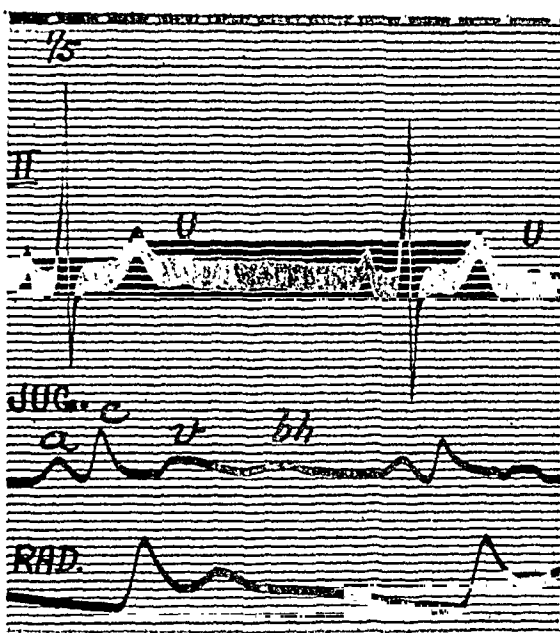
FIG. 12.—Combined electrocardiogram, jugular, and radial tracing.   U coincides with the fall
of " v " ; and occurs long before the " b h " wave.

or downstroke of " v " can be established.   Its appearance in the early stage of diastole, and its evident time relation with " v " exclude any relation between U and the " b h " wave of the venous tracing which does not appear until late in diastole.   It is found only in slowly acting hearts and is due to the floating up and transient closure of the tricuspid valves when the blood flows into the ventricle (Mackenzie, 1925).   The first part of diastole has been termed by Luciani (1911) active diastole.   Lewis (1925) refers to the second part of diastole, after the opening of the A–V valves, as diastasis.   Even assuming a remnant of muscular activity in the first part of diastole, i.e., the post-sphygmic period that is the interval between the closure of the semilunar and the opening of the A–V valves, this could not be represented by the U wave ; for its appearance after the opening of the A–V valves (the peak of the venous " v " wave) rules out this explanation.

The simple fact of U often beginning before the end of T, so as to deform it (Figs. 2 and 3), suggests at once that it can begin before systole is over, accepting the end of T as the end of systolic contraction.   In the U wave we seem to have an electrical component, independent of both systole and diastole, arising sometimes before and sometimes after the end of T.   Simultaneous records of

the end of T with a phonocardiogram of the second heart sound might help to decide, were U waves present in such a combined record.

A certain similarity between the shape and direction of T and U and their similar response in experiment seem to suggest that they have a common origin, or at least that U is derived in some way from the T wave. Strongly against this explanation, however, is the common appearance of U in brady-cardia on the descending portion of T, i.e., before systole is over. As the end of T marks the end of systolic contraction, U might be a sequel of that con-traction. Nahum and Hoff (1939) in this sense speak of U as the expression of the phase of recovery, after the refractory period. If so, U on this hypothesis should always have a direct time relation to T or to the end of T. But the facts are to the contrary : U may as easily deform T as follow it, according to the simple factor of rate. The truth is that U is related in time to QRS and not to T. Once the Q-end T period is determined, a period which varies chiefly with rate, U may be recognized as : (a) a hump on the downstroke of T, at a rate below 60, i.e., when the Q-end T period exceeds 0·40 sec. ; (b) an isolated wave, upright or inverted, at a normal or moderately high rate (60 to 110), i.e., when the Q-end T period is from 0·40 to 0·34 sec. ; (c) partially or totally fused with the succeeding P at a rate above 110, i.e., when the Q-end T period is 0·34 sec. or less. The contrast lies between the relative fixity of the Q–U period, measuring 0·38–0·42 sec., and the variability of the Q–T period measuring between 0·34 and 0·46 sec. at different heart rates. The idea that U disappears with change of rate is incorrect. When it is not identified as a separate wave, it still may be present, fused with the succeeding P and elevating it correspondingly (Fig. 1).

Though existing hypotheses advanced to explain the U wave have been criticized and even rejected, I am unable to offer anything more satisfactory. Its closer time relation with the QRS complex than with T, and its beginning, sometimes before and sometimes after systole is completed, seem to exclude simple or direct relation to the muscular contraction of the heart. The U wave may represent an electrical event in the heart muscle, so far novel and unrecog-nized, which is not the expression of a kinetic activity and so not directly related to the heart rate.

SUMMARY

Observations have been made on the incidence, appearance, and variations of the U wave of the human electrocardiogram in health and disease ; and its genesis is discussed.

1. *The U Wave in Health*

In about 70 per cent. of normal records U is present in one or more limb leads, and in about 5 per cent. it is at least 0·5 mm. in height. It is often larger in special chest leads, especially in IV R, in which it may be 0·25 to 2·0 mm. high and 0·18 to 0·24 sec. in duration.

In tachycardia, it is fused with the succeeding P. In bradycardia with its lengthened S–T period, it overlaps T, forming a hump on its descending portion.

It follows that U is related in time to QRS and not to T ; it tends to fuse with T when the Q–T period is longer than 0·40 sec. It varies with respiration, becoming sharper and shorter in inspiration, and flatter and longer in expiration. It enlarges after exertion and in forced apnœa. Vagal release by atropin influences it little if at all ; vagal stimulation (e.g., by carotid sinus compression) may exaggerate or may dissipate the wave.

2. *The U Wave in Disease*

Of 100 consecutive electrocardiograms in which U was higher than 0·5 mm. in limb leads, nearly half the patients had a blood pressure above 160 mm. and 40 per cent. showed enlargement of the left ventricle on radioscopy. A large U was less often seen with right ventricular enlargement. U tends to be absent in heart failure and may first be seen during recovery from it. Digitalis can enlarge a small U wave or produce one where none was seen before its administration. Though T and U may enlarge concurrently, there is otherwise little relation between them ; for instance, a large T may have a small U wave following it or vice versa.

An inverted U wave is the only pathological form yet recognized. It is to be found in coronary thrombosis, hypertension, angina pectoris, and aortic incompetence. Generally, it is found with an inverted T, though it can be the only pathological sign in an otherwise normal record.

After extrasystoles commonly, and in bundle branch block rarely, U may be seen, either upright or inverted. Where T is bifid, as occasionally it is, the identification of U may not be easy.

3. *Interpretation of the U Wave*

The idea of its extracardiac origin is untenable. The U wave is a product of cardiac contraction and has generally been held to occur after contraction has ceased, i.e., in diastole. At normal heart rates it appears early in diastole and coincides with the peak or the fall of the jugular " v " wave, i.e., while the A–V valves are open and therefore after systole is complete. It occurs well before the " b h " venous wave. Yet as the U wave in bradycardia begins before, and at a normal rate after the end of T, and in tachycardia is fused with the succeeding P, U may be envisaged not only as a more persistent wave than had been thought, but as an electrical event independent of both systole and diastole. The R–U period is relatively constant while the R–T period varies greatly with rate. This constant relation of U to R, the lack of relation of U to T, and the fact that a mere change in heart rate makes it seem at one time systolic and at another diastolic, render doubtful the interpretation of U either as a wave arising from muscle going out of contraction or as the electrical expression of a supernormal recovery phase.

Possibly U has a hitherto unknown quality in that it appears unattached to systole or to diastole, for it is independent of T and also curiously independent of the heart rate.

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THE PSYCHOLOGICAL TREATMENT OF CASES WITH CARDIAC PAIN

BY

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In two papers published in 1937 (*The Lancet*, pp. 609 and 665) an attempt was made to assess the relative significance of emotional and organic factors in the production of cardiac pain. On examination of two groups of patients it was shown that four fifths of the first, i.e., patients with cardiac pain, as compared with one fifth of the second group, i.e., patients with cardiac deficiency but without pain, suffered from some psychological disorder before the appearance of cardiac symptoms. In a surprisingly high number of cases the cardiac pain seemed to emerge as a late component of a chronic anxiety state and its onset was often precipitated by some disturbing event in the patient's life. This sequence is familiar as far as functional pain is concerned, but it was also found in certain cases of angina of effort.

In continuance of these studies, a group of 12 patients with cardiac pain has been submitted during the past two years to psychological treatment, to find to what extent patients with functional cardiac pain might respond to this treatment, and if and how far cases of angina of effort, carefully selected because of a prominence of emotional problems in their histories, might be amenable to psychotherapy.

MATERIAL : SELECTION OF CASES

Seven patients complained of the type of pain previously described under the label angina innocens (*Brit. Med. J.* 1937, I, 695). Reference to that paper will make it clear that a cardiac condition, not an intercostal fibrositis, is referred to. For the purposes of the present paper the less controversial terms functional pain or functional cardiac pain are used; another synonym is left submammary pain.

Angina of effort has as its basic lesion coronary disease, but the degree of pain is proportional to the predisposition of the nervous system to make this manifest. Psychological treatment is thus rational in cases of angina of effort with psychological abnormalities.

Seven patients with functional pain, two men and five women, and five men with typical angina of effort form the basis of the present study. One

was a patient of Dr. Evan Bedford and the others were examined clinically and sent for treatment by Dr. Geoffrey Bourne. These cases have been selected with considerable care ; previous to treatment they had all been examined carefully and had been followed for lengths of time varying, in the functional cases, from one to four years and, in the patients with angina of effort, from two to thirteen years. The type of pain had been analysed according to the classification previously described (*Brit. Med. J.*, 1935 I, 1109). During the period before psychological treatment the diagnosis had thus been confirmed by many examinations. A number of patients were referred to Dr. Wittkower for an opinion as to their suitability for treatment and were rejected for reasons that will be explained later.

The clinical material fell into two groups, according to the type of pain present. In the group with functional pain were four cases with normal hearts, one with hyperpiesis, and two with mitral stenosis ; in the angina of effort group were two with no other severe cardiovascular abnormality, two with hyperpiesis, and one with aortic stenosis. The cases are summarized as follows.

PATIENTS WITH FUNCTIONAL PAIN

Case 1. A man, aged 54, had suffered from persistent severe pain in the left chest for three years. He had collapsed and fainted at the onset of the pain, and since then had complained of pain in the chest, radiating to the left arm. This was not quantitative to exertion or diminished by rest, but he was seen by a physician who told him that he had ' angina' and stopped him from working. On examination no cardiovascular abnormality was found, the electrocardiogram was normal, and the history of the pain was of the functional type. He was therefore reassured with regard to his heart and was referred for a psychological opinion and treatment. (See later.)

Case 2. A woman of 28, with early mitral stenosis, had for three years suffered from pain which had, at times, been very severe. It was on the left side of the chest and was worse when she was tired. She had suffered also from attacks of pain followed by faintness, although she did not lose consciousness. In such an attack she would feel as if the end had come. On examination there was an early mitral stenosis, confirmed by X-ray, but the electrocardiogram was normal.

Case 3. A woman of 22 had for the previous five years felt pain on exertion on the left side of the chest radiating to the neck and arm. It was increased after exertion but not during it, and was accentuated by worry and fatigue. There was no cardiovascular abnormality except slight accentuation of the first sound.

Case 4. A woman of 43 had suffered for some years from pain in the left side of the chest which was at first a severe sudden stab followed by a dull ache persisting for a few minutes. Subsequently it became more persistent but was never proportional to exertion. On examination there was marked enlargement of the heart, both to the right and to the left, mitral stenosis, and auricular fibrillation.

Case 5. A man of 39 had suffered from palpitation and exhaustion for three years. Exercise produced pain in the left side of the chest which was not quantitative to exertion. On examination he was found to have a blood pressure of 180/130. The electrocardiogram showed left-sided preponderance.

TABLE I

PATIENTS WITH FUNCTIONAL PAIN

Case number	Age and Sex	Diagnosis	Duration of Treatment		Result of Treatment		Follow-up	
			Physical (in years)	Psychological (in months)	Pain	Psychological symptoms	Duration (in months)	Results
1	54, M	Conversion hysteria	3	4	Lost	Lost	12	No complaints ; at work
2	28, F	Anxiety state, and mitral stenosis	10	3	Lost	Much improved	18	No complaints ; at work
3	29, F	Conversion hysteria	1	4	Lost	Much improved	12	No complaints
4	43, F	Anxiety state, and mitral stenosis	2	4	Lost	Much improved	18	Relapsed after 6 months with failure
5	39, M	Anxiety state, character disorder, and hyperpiesis	5	4	Lost	Much improved	6	Death after 8 months
6	28, F	Character disorder	4	4	No change	Unchanged	5	Improved later and at work
7	32, F	Conversion hysteria	2	9	Lost	Much improved	1	At work

Case 6. A woman of 28 had suffered from severe shortness of breath on exertion for years and also from severe attacks of pain that might come on at any time and pass down the arm. These might be accompanied by faintness. In addition, she had a persistent left-sided ache which was worse after exertion and also passed down the left arm. On examination there was mitral stenosis with a regular rhythm.

Case 7. A woman, aged 32, had suffered for two years from pain in the left side of the chest, which was worse on exertion and was accompanied by palpitation and a feeling of weakness. On examination there was no abnormality except for a systolic murmur at the apex, conducted to the pulmonary base.

PATIENTS WITH ANGINA OF EFFORT

Case 8. A man of 54 had for 10 years suffered on rare occasions from a slight pain, central in position and substernal. This came on only after digging, sawing, or similar strenuous exertion. He had been examined several times and had been told that he had heart disease, which was probably due to rheumatic fever in the past. A year before he was first seen he began to get pain frequently

on exertion, which would go with resting and was quantitative to the amount of exertion.   It was never present at rest.   On examination the apex beat was just outside the mid-clavicular line and was forcible.   A harsh loud systolic murmur was present at the aortic base, with a systolic thrill, and the murmur was also heard at the apex.   The blood pressure was 150/110.   He remained under observation for two years before he was referred for psychological treatment.

Case 9.   A man of 65 had suffered for two years from a retrosternal pain that only came on as he walked and was proportional in its severity to the amount of walking.   It was not increased by emotion, but was always accentuated by hills.   On examination there was no increase in the blood pressure, but the apex beat was slightly displaced to the left, the heart/chest ratio being 14/27 cm.   The electrocardiogram showed left-sided preponderance and some notching in the R wave in lead II.   (See later.)

Case 10.   A man of 49 had had pain in the chest on exertion for two years ; it was central in position but did not radiate to the arms.   This was quantitative to the amount of exertion but was also brought on by excitement.   Six weeks before he had had a severe attack of pain on getting out of bed, upon which he fainted.   It lasted on and off severely for a week.   Since then he had been slowly improving.   He was then watched for a period of two months, during which the pain remained unchanged in degree.   On examination he had severe hyperpiesis, 235/140 mm., the heart showed no clinical enlargement and the sounds were normal.   The electrocardiogram showed no abnormality. (See later.)

TABLE II

PATIENTS WITH ANGINA OF EFFORT

Case number	Age and Sex	Diagnosis	Duration of Treatment		Result of Treatment		Follow-up	
			Physical (in years)	Psychological (in months)	Pain	Psychological symptoms	Duration (in months)	Results
8	54, M	Aortic stenosis, hyperpiesis, anxiety state	4	4	Lost	Improved	18	No pain for 6 months ; then relapse with erysipelas
9	65, M	Reactive depression	3	3	Lost	Improved	12	No pain for 6 months ; some recurrence, but slighter and less frequent
10	49, M	Hyperpiesis, anxiety state	2	10	Much improved	Improved	7	Occasional slight pain ; other symptoms better
11	51, M	Anxiety state	2	2	Improved	Improved	3	Much improved
12	49, M	Hyperpiesis	13	8	No change	No change	3	Unchanged

Case 11.   A man of 51 had had pain that was quantitative to exertion for two months.   The onset had been gradual and the pain was not present at rest. The pain was of a squeezing nature and radiated down to both forearms.   It was worse on walking uphill and caused him to stop and might last up to two minutes.   He had had two slight attacks in bed.   The electrocardiogram showed flattening of the T wave in leads I and IV.   During a period of four months, while under treatment as an out-patient, his symptoms became slowly worse. He was, therefore, referred for psychological treatment.

Case 12.   A man of 49 had felt slight pain on the left side of the chest for sixteen years.   This was at first of the functional type, being left-sided, radiating to the left arm and elbow, but having no relation to exertion or emotion.   It might persist for variable lengths of time up to several hours and was not relieved by nitroglycerine.   One year previous to examination he had an attack of angina of effort, the pain now being strictly quantitative to exertion and disappearing when exertion slowed down or ceased.   Since then he has had angina of effort of a moderate degree.   Six years before his systolic blood pressure was 150, but two years before it had risen to 210/110.   On examination the heart showed slight enlargement and there was a systolic murmur at the apex.   The blood pressure was 210/138.   The electrocardiogram was of the low voltage type and showed some slurring and widening of the QRS complex.

Nature of Psychological Treatment

Short methods of treatment have been employed in these twelve patients. Each was seen three times a week for an hour.   With a few exceptions, the treatment was limited to 60 hours.   In some cases, superficial discussion of the current conflict was found to be sufficient to relieve the complaint.   In most cases, however, the treatment was conducted along analytical lines, i.e., by free association while lying relaxed on a couch.   The aim of such treatment is to help the patient to bring out and to face attitudes, previously un-recognized, which are often strongly emotional.   As serious cardiac disorders were present in many of the patients, severe emotional shocks were avoided by keeping interpretation on a comparatively superficial level.

Co-operative patients with a mild or moderate psychological disorder were preferably taken on for treatment.   Advanced age, complaints of very long standing, a low standard of intelligence, as well as evidence of a very severe psychological disorder were generally considered as contra-indications.   In the group with functional cardiac pain, the psychological diagnosis was labelled as an anxiety state in three patients, as conversion hysteria in three, and as a character disorder in one.   Four patients with angina of effort suffered from anxiety states, in two of them with a pronounced obsessional background, and one patient from a reactive depression.

Results on Discharge and After Follow-up

1. *Functional Type of Pain*

There will be very little argument about the indication for psychotherapy in patients with cardiac pain of the functional type.   Most cardiologists, in

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these cases, employ some form of psychotherapy in an open or concealed form. A glance at Table I shows that, before the beginning of psychological treatment, the patients had received physical treatment of about two or three years—in one case for ten years—without much benefit. The results of psychological treatment can be summarized as follows.

(a) *Cardiac Pain.* After an average of four months of psychological treatment, six of the seven patients had lost their cardiac pain.

(b) *Occupational Efficiency.* Three patients who were incapacitated by their complaint, returned to work at the end of the treatment.

(c) *Psychological Complaints.* Their nervous symptoms, e.g., anxiety, shaking fits, etc., were improved or completely relieved.

(d) *Follow-up.* In four cases this covered a year or more, and three patients kept up their recovery over the whole period of observation. One was completely restored for six months, but had a relapse in connection with decompensation of the heart ; another, after six months of apparent health, died of acute uræmia. In one, who did very well under treatment, the follow-up is too short. The only patient who did not respond improved during a further course of treatment by Dr. Crichton-Miller, under evipan administration.

2. *Angina of Effort*

Five patients with angina of effort (Table II), after physical treatment without much avail over several years, were taken on for psychological treatment. The results can be summarized as follows.

(a) *Cardiac Pain.* Two of them, who before treatment were hardly able to walk 100 yards without an attack, were completely relieved from pain at the end of the treatment ; two were improved ; and one was not amenable to treatment.

(b) *Occupational Efficiency.* In two patients occupational efficiency was restored under treatment.

(c) *Psychological Complaints.* With one exception the patients reported an improvement of their nervous symptoms.

(d) *Follow-up.* This, as should be anticipated, is less satisfactory than in the functional group. The two patients that lost their pain under treatment remained free for six months ; afterwards, one relapsed in connection with erysipelas and the other noted a slight return of pain. " I get the pain only occasionally," he says in a letter, " instead of frequently, and the pain is less when it does occur than it was formerly." The two improved patients kept up their improvement. One did not respond to psychological treatment.

ILLUSTRATIVE CASES

The points at issue are best illustrated by some typical instances.

Case 1. A big, loquacious, simple-minded man, aged 54, had suffered from attacks of cardiac pain for over three years—" like a knife stabbing." The pain extended along the left arm and was brought on by hard work, excitement, and worry. He was admitted to a hospital, where he was told by one of the physicians that it was angina

pectoris and that he should avoid any exertion. Since then he had been out of work, resting at home ; he could not walk 100 yards without the pain starting. For the past twelve months he had been sitting in a chair, hardly ever leaving his ground floor room. The physical diagnosis was functional type of cardiac pain.

The youngest of nine children, he was spoilt and pampered as a child. He was his mother's special favourite and from early childhood was over attached to her. He declined to marry as long as she lived, although she urged him to do so. After her death, when he was 28, he had a serious nervous breakdown, but married a year later.

He had worked as a parquet-floor layer. When 47 he began to worry more about his work, because there was a new manager who wanted the work to be done more cheaply. As a foreman with a higher wage, he had to work harder than the others and he worried day and night about getting the sack. Very often he could not sleep, and developed headache, giddiness, and morbid fears of crowds and enclosed spaces. " I worried until I collapsed." About two years ago he collapsed at work and immediately afterwards his attacks of heart pain started.

After four months' psychological treatment, his pain disappeared and he returned to his work. Since then he has been free from any complaints. " I walk and enjoy it. My wife grumbles that I walk too quick. I sleep well and awake refreshed. There's a brighter atmosphere all round."

Case 9. A retired schoolmaster, aged 65, a pleasant, friendly, compliant Lancashire man, began to have typical attacks of angina of effort three years ago. He was seen by various heart specialists and told to avoid any exertion. He was unable to walk any distance without attacks of cardiac pain setting in. He had worked his way up from great poverty to be an assistant schoolmaster. In 1928, after quite a successful career, he had to leave as a newly appointed headmaster insisted on his dismissal. After that a hard struggle began ; being advanced in age, he only got temporary posts and eventually, three years ago, found it impossible to get a job at all ; his savings were used up and, unable to support himself, he became entirely dependent on his son. About this time his attacks of angina of effort started.

Superficial discussion of his conflicts was sufficient to relieve his complaints. For six months he remained free from pain, after which slight occasional pain returned.

Case 10. A silversmith, aged 49, attended hospital because of violent attacks of pain in the middle of the chest. He had had these for over two years, brought on by heavy meals, excitement, or the slightest exertion. The diagnosis was angina of effort and hyperpiesis.

He was a courteous, unassuming, little man, self-conscious and blushing easily ; in contrast to his docile and almost timorous behaviour, however, he was harassed by what he called aggressive thoughts. He had impulses to punch people or to spit at them or to cut his wife's throat and, although he never did, was haunted by the fear that he might give way to these impulses and might be locked up and hanged. Further exploration revealed that he had been a most aggressive, troublesome baby but his aggressiveness had been nipped in the bud by a stern, dogmatic father. Rarely, and then only at the peak of resentment, did the patient display aggressiveness in any shape or form.

All through his life he has been rather touchy about any encroachment on his independence, and never liked to be dictated to by anybody. Frequent arguments with his wife arose because he rather emphatically insisted on being " governor in the house." In contrast to this, in recent years he has developed a fear of being thought effeminate and an urge to touch the private parts of a man. Any innuendo in this direction or even discussion of the subject of homosexuality made him blush violently. During the past two years he has been impotent and, in fact, owing to a pronounced fear of going out and of collapse, he has got into a state of complete dependence on his wife. He gave up his job, his wife kept and nursed him and he would never leave the house unless she accompanied him.

Investigation revealed that as the eldest of nine children he had been his mother's

favourite and, whereas he was over-attached to her, he was scared of, and strongly resentful of, his father. One·incident, which he said he had never·got over, stood out in his memory. His mother was being confined when he was five or six years old ; he had heard her groaning and wanted to find out why she was doing it but his father pushed him out of the room.

At about 18 he started to masturbate and about the same time to drink. His father was against his drinking and said that he would have to pay for it. After some months he broke down completely ; he cried incessantly, was afraid to go out and developed a fear of insanity. This condition passed off after several weeks. Twelve years ago he had a second nervous breakdown. His fears of going out and of insanity returned and he refrained from sexual intercourse for two years, as he thought this might drive him mad.

Two years ago his mother died and her death initiated his third nervous breakdown. Since then the attacks of cardiac pain, the impotence, and various psychological complaints have developed. " I still want to hang on to my mother and to ask her if to do something will be all right."

As the patient faced up to his previously unrecognized attitudes, the attacks of cardiac pain gradually got less frequent and less severe. He returned to work, his potency was restored, and his nervous symptoms have greatly improved.

COMMENTS AND CONCLUSIONS

The data obtained confirm the view put forward previously, that in cases of functional cardiac pain the pain is nearly always due to transformed anxiety arising from a conflict, unusual in intensity and abnormal in type, between menace to vital feelings and existence on the one side and self-preservation and self-assertion on the other. It is almost a truism to state that those harassed by anxiety are more apt than others to develop cardiac pain, if for some reason or other they are affected by some cardiac disorder. Both in cardiac pain of the functional type and in true angina of effort, relief of underlying anxiety by psychological treatment results in improvement or loss of cardiac pain.

As should be expected, psychotherapy has very little or no effect on the organic cardiovascular disease, the blood pressure and cardiac condition remaining unchanged ; it could, therefore, be objected that removal of pain, as it removes the essential warning not to overdo physical exertion, may be injurious. However, none of the patients with angina of effort died during the prolonged follow-up period and, in fact, as the anginal attacks may in part be due to spasm of the coronary arteries, removal of these attacks may result in an improved circulation in the coronary system.

Summing up, it has been suggested that patients with the functional type of pain and certain patients with angina of effort derive benefit from psychological treatment. The diagnosis of cardiac pain of the functional type is an indication for psychological investigation and possibly for systematic psychotherapy. Only in certain cases of angina of effort, carefully selected as in the cases quoted because of a prominence of emotional elements, is an attempt at psychotherapy justified.

ANALYSIS OF FIFTY NORMAL ELECTROCARDIO-GRAMS INCLUDING LEAD IV

BY

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An analysis of the electrocardiograms of 50 normal women students between the ages of 20 and 27, attending the Royal Free Hospital, is given. Originally the records of 100 students were taken, but later it was decided to select 50 that showed a normal relation between weight and height and were physically fit. Special attention was directed to lead IV and its possible relations to the three standard leads. In all our work lead IV R has been used, i.e. left arm electrode at the extreme outer border of the apex beat as the exploratory electrode and right arm electrode as the distai indifferent electrode, this following the recommendations of the joint report of the Cardiac Society of Great Britain and Ireland and the American Heart Association in 1938.

It is proposed to analyse the duration, form, and amplitude of each wave. A number of tables, frequency curves, percentage relations, and mean values have been constructed for these in each lead ; only a few of them have been selected for reproduction in the text.

THE P WAVE

All the measurements given in the text have been made according to the standard method except where otherwise stated. The earliest accurate measurements of the amplitude and duration of the P wave were made by Lewis and Gilder (1912) and by Goodall and Richards (1914).

Form. Table I shows that this is very variable, the round and pointed forms being most prevalent. The large preponderance of the pointed shape in lead II and the great variation in lead III are also noticeable. Bifid waves were found only in lead I. In two records the form was not the same in each cycle, varying between the pointed and round shape. We cannot give a satisfactory explanation of the factors responsible for the variation from cycle to cycle, and one must assume that in every cycle the excitation wave follows a slightly different path. At the same time the summation of the electrical activity of both auricles is not symmetrical and smooth. As a result the P wave curve changes its form from round to notched, bifid, or pointed.

TABLE I

FORM OF P WAVE IN 50 CASES (PERCENTAGES)

Form	Lead I	Lead II	Lead III	Lead IV
Round	36	24	32	56
Pointed	50	70	38	40
Round or pointed ..	—	6	8	2
Inverted	—	—	12	2
Bifid or flat	14	—	10	—

Shipley and Hallaran (1936), in an analysis of the electrocardiograms of 200 normal men and women, recorded smooth and round P waves in 67 per cent. and pointed in 33 per cent. Notching was present in 30 per cent., but only in one record was it found in all leads. P was inverted in 5 per cent. of their records, but only in lead III. A diphasic P was met once in lead II and 32 times in lead III. When P was inverted, T was also inverted; and when P was diphasic in lead III, T was also diphasic. We found a similar relationship, but in one record P was inverted in lead IV and T was upright. In subsequent tracings inversion of P was noted in other leads or cycles, whereas in lead IV the auricular deflection was upright. This was a case of wandering pace maker. The association of the amplitude of P greater than 2 mm. and notching was not met with in our cases, nor in those recorded by Shipley and Hallaran, and we agree with them and others that this association is one of the signs of mitral stenosis.

Amplitude. Originally Lewis and Gilder gave the following values for the P wave deflection in 52 healthy subjects; lead I=0·52 mm., lead II=1·16 mm., and lead III=0·81 mm. More recently Burnett and Taylor (1936) gave an analysis of 1276 electrocardiograms taken from 167 children, aged 3 weeks to 12 years, of whom 85 were boys and 82 girls. The amplitude was higher than in adults (upper limit 2·5 mm. and lower limit 0·5 mm.). The girls showed a higher amplitude than the boys, but after the age of ten there was less variation in all leads. In résumé the authors state that P showed higher and lower deflections in children than in adults, more frequently high in girls than in boys, but that the average did not show any notable departure from the average value found in the adult.

Shipley and Hallaran give the average amplitude of the P wave for men as 1·41 mm., and for women as 1·30 mm. in lead II, which showed the greatest deflection of P in 90 per cent.

In comparing the average value of our 50 students, we found much higher figures than those given by previous investigators (see Table II). The mean value of P in the four leads was 1·74 mm. ; and the greatest value, in lead II, 2·3 mm. The maximum and minimum deflections of P in our records were 5 mm. and 0·5 mm. This shows that large P waves occur quite often and have no abnormal significance. The highest average deflection was found in lead II, and the next in lead IV.

TABLE II

AMPLITUDE OF P WAVE IN 50 CASES (PERCENTAGES)

Range of Amplitude in mm.	Lead I	Lead II	Lead III	Lead IV
0–1	6	—	24	2
1–2	72	36	48	58
2–3	20	38	26	34
3–4	2	18	2	6
4–5	—	8	—	—

Duration. Our measurements for the duration of the P wave fit in to some extent with those of other investigators and with those of Shipley and Hallaran, who give the value of 0·08–0·12 sec. for the duration of P for men and women alike. Their average is 0·09 sec. and the longest duration 0·12 sec. The average values found by us were 0·08 sec. in each lead, except in lead I where it was 0·07 sec. ; and the mean value for the four leads was 0·076 sec. This value is lower than that reported by the above mentioned investigators, and our view is that in young women the duration tends to be shorter than in men. From our measurements it appears that there is no definite relation between the amplitude and the duration of the P wave.

THE P–R INTERVAL

P–Q Duration. This was measured from the end of P to the Q deflection The mean value for each lead was 0·06 sec., except in lead III where it was 0:07 sec.

The mean value for the four leads was 0·064 sec. The longest duration was in lead III, 14 per cent. being between 0·09 and 0·12 sec., and 70 per cent. between 0·06 and 0·09 against the 50 per cent. in the other leads. In comparison with the values exhibited by the normal heart, cases of mitral stenosis tend to show a short P–Q duration.

P–R Interval. The value of the P–R interval 0·13–0·21 sec. established by

TABLE III

DURATION OF P–R INTERVAL IN 50 CASES (PERCENTAGES)

Range of duration in seconds	Lead I	Lead II	Lead III	Lead IV
0·09–0·12	22	4	6	6
0·12–0·15	58	50	32	54
0·15–0·18	16	42	52	38
0·18–0·21	2	4	6	2
Mean value (seconds) ..	0·13	0·14	0·15	0·14

Lewis and Gilder (1912) has been adopted beyond criticism as a normal range. Lewis showed that for cats it is 0·06–0·08 sec., and for dogs 0·08–0·10 sec. Paul

White in his book gives the normal value for adults 0·20 sec. (average 0·16 sec.) and for infancy and childhood 0·08–0·18 sec. (average 0·125 sec.). The results of our analysis of P–R are reproduced in Table III, and the frequency curves in Fig. 1. The range of duration was between 0·09 and 0·21 sec. In lead I most cases fell within the range 0·12–0·15 sec., with a large number of small duration,
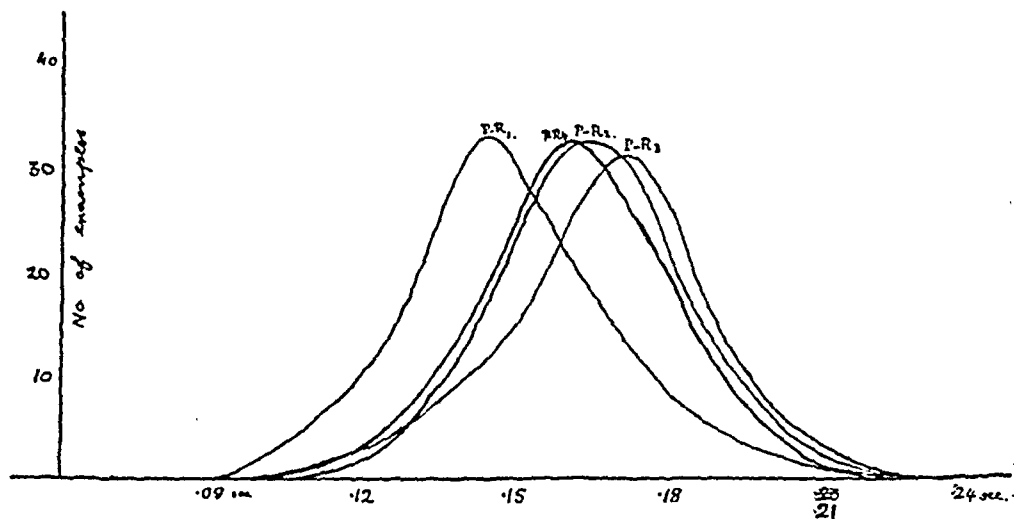

FIG. 1.—Frequency curves of the duration of the P–R interval in the four leads.

0·09–0·12 sec. In the other three leads the greatest number of cases were between 0·12–0·18 sec.

THE QRS COMPLEX

The most variable part of the QRS complex and that on which a considerable number of investigations has been published, especially in relation to coronary disease, is the initial ventricular deflection, the Q wave. The first wave of the ventricular complex is designated as Q by Einthoven, if it points down, and as R if it points upwards. S denotes the downwards wave that comes after the upward R, and where there is no upward wave the downward wave is designated as S. Lewis in his book (1925) states that Q is "beyond question a ventricular event, occurring as it does in curves of complete dissociation of auricle and ventricle as part of ventricular complex, as was first pointed out by Einthoven." If QRS is inverted, as in dextrocardia or in abnormal axis deviation, Q and S will also be inverted and point upwards. Besides that, as we shall see, there are normal curves in which the initial ventricular deflection is such that it is difficult to distinguish Q and whether it points downwards or upwards. Sometimes Q is absent or flat or represented as a thickening at the beginning of the R wave, in which case it is called fused. Finally Q may be replaced by an initial diphasic phase at the beginning of the R wave. The electrocardiograms, Fig. 2, A and B, are examples of "inverted" Q according to some American authors ; Fig. 2C is an example of Q fused to R, or flat ; and Fig. 2D is an example of "diphasic" Q.

Paul White (1937) states that Q is usually absent in lead II or may be a

short point, projecting 1–2 mm. below the base line, and that in infants and young children it may form a more appreciable part of the QRS complex being as much as 3–4 mm. in amplitude. In lead I, according to him, the QRS complex is such that it is often impossible to tell whether we are dealing with an upright Q, an inverted R, or an upright S, and such variations certainly occur in some cases.
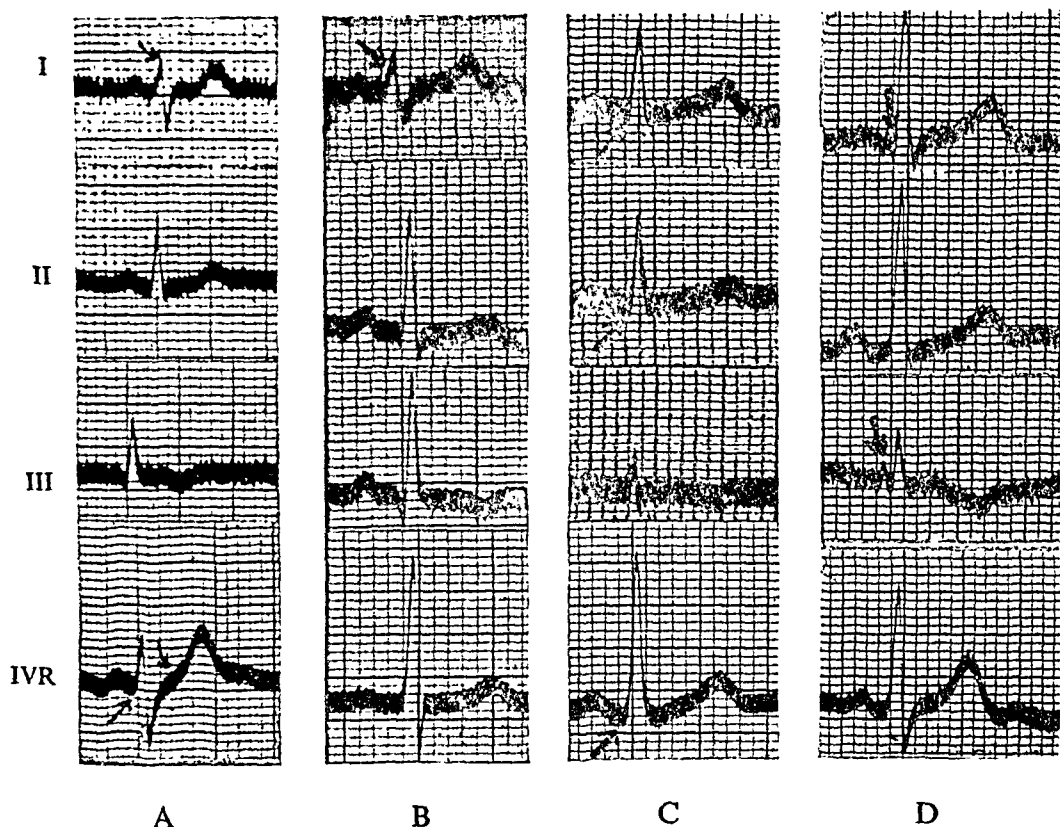
FIG. 2.—Cardiograms selected to show different types of deflections discussed in the text : (A) and (B) show inverted Q in lead I ; (C) shows Q fused to R ; (D) shows diphasic variation of Q in leads I and III.

Pardee (1933) has drawn attention to a deep Q_3 as an indication of myocardial disease. Kossman, Shearer, and Texon (1938) affirm that normal subjects with a deep Q_3 rarely show the other criteria of Pardee. In a combined series of reports from Lewis and Gilder, Cohn, Master, Pardee, and Edeiken and Walwerts a deep Q_3, according to the above criteria, was found twice in the electrocardiograms of 1102 young men, including 116 normal athletes.

We have investigated Q_3 according to Pardee's criteria in all our cases. A deep Q_3 was of frequent occurrence and was more frequent in young women and children than in adult males. But in no electrocardiogram did we find the Pardee criteria followed, except in one (Fig. 3C). It is from a woman, 21 years of age, who shows clinically no heart abnormality and is in perfect health. There is a deep Q_3, of over 4 mm., which is more than 25 per cent. of the

largest QRS complex in any lead.   There is also a conspicuous Q in leads I
and II and low voltage in lead IV.   The arrow in the record is pointing to
show " fusion " between S and R in lead III, according to the interpretation
of Hurxthal and others.   There is also an inverted or isoelectric P wave and
an inverted T in lead III.   We consider this electrocardiogram is a rarity
because it follows Pardee's criteria although it is from a normal person.

We feel that unless we know all the possible variations of Q in normal
persons it is difficult to accept with confidence its diagnostic value as suggested
by the American investigators in coronary infarct.   Table IV shows the analysis
of the form of Q deflection.

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TABLE IV

FORM OF Q WAVE IN 50 CASES (PERCENTAGES)

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Form	Lead I	Lead II	Lead III	Lead IV
Down (or down -fused or -diphasic)	52	64	50	24
Upright * (or upright-fused) ..	4	—	16	4
Flat * (or flat -fused or -diphasic)	44	36	34	72

* The terms upright, flat, fused, or diphasic, are adopted from the works of certain Ameri-
can authors, e.g. Hurxthal, but their acceptance is not yet general.

Recently Kossman, Shearer, and Texon (1938) have reported the detailed
study of the incidence and quantitative relationship of the Q deflection of the
three standard leads of the electrocardiograms of 178 normal subjects in order
to find a standard for comparison for any type of heart disease.   In either the
sitting or recumbent position and during either phase of respiration, 40 per
cent. showed a Q deflection in lead I, 60 per cent. in leads II or III, and 40 per
cent. (or slightly less) in both leads II and III.

R Deflection.   The R wave follows immediately the initial ventricular
deflection.   According to the general view it is composed of two projections,
an upright which starts from Q and a downwards which ends in S, the final
deflection.   The amplitude of R in our curves was measured from the isoelectric
line to the summit, and the slight or deep downwards deflections produced by
Q or S were ignored.   However, in some records especially in lead III, R is
diphasic or may take the shape of M or W.   The R deflection is considered
diphasic when the projection, instead of starting from a downward or flat Q,
starts from an upright (inverted Q) and finally goes downwards to a deep
S wave.

The diphasic R should not be confused with an inverted R met with in left
or right preponderance.   In this case the R deflection starts from the isoelectric
line from an inverted Q, projects downwards, and then ascends back to the
isoelectric line to an inverted or fused S wave.   A diphasic R has a positive phase
which is above the isoelectric line and a negative phase which is underneath

the isoelectric line. This interpretation is not generally accepted, but we consider it necessary. In some records the positive part of a diphasic R is very small on account of a big initial Q inversion (see Fig. 2B). In other records it starts from a smaller inverted Q and descends to a deep S (see Fig. 2A, leads I and IV). However, it is sometimes very difficult to differentiate between a diphasic R wave and an inverted Q wave. For example, in Fig. 3A in
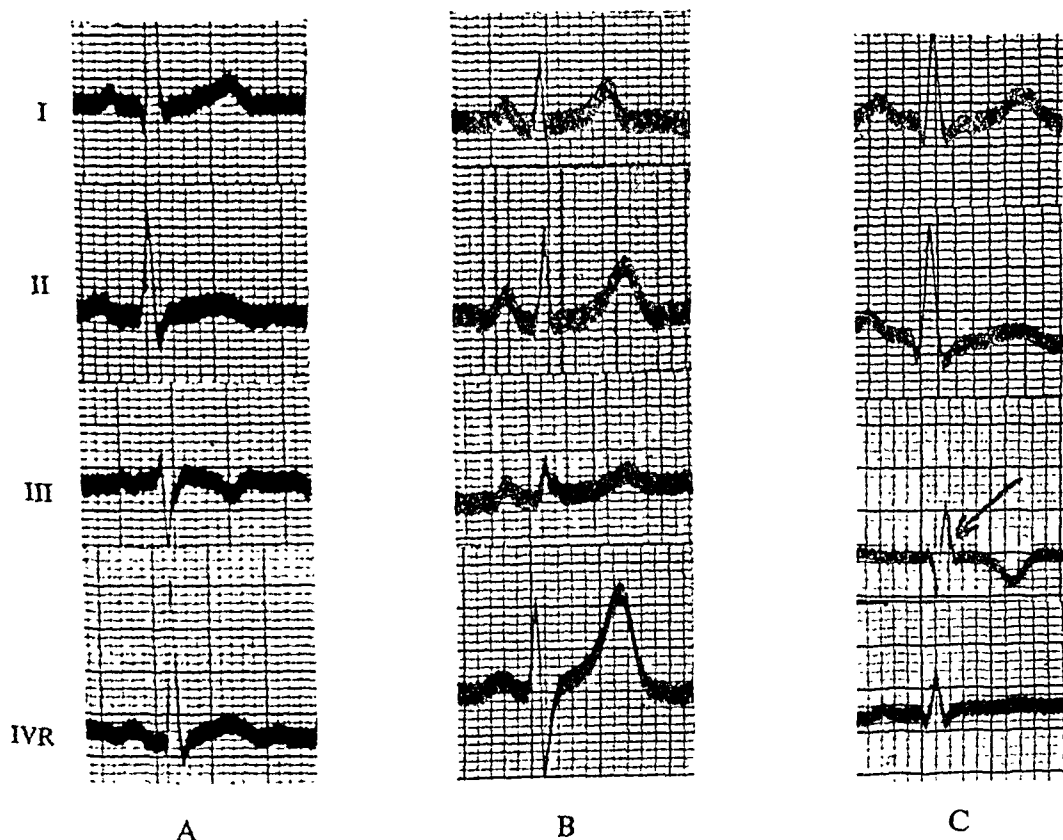

Fig. 3.—(A) Upright Q in lead III : (B) S fused in lead III when Q is fused or upright in lead I : (C) Example of Pardee criteria found in a normal subject.

lead III there is an upright Q and an inverted R, but there are no other signs of left preponderance. The R wave in lead II is not diphasic and there is a medium projection of R in lead I. The record is from a young student who is a good athlete. All that can be said is that she has a well developed left ventricle.

The relation between Q in lead I and S in lead III is considered significant. In our records it was found that almost always when Q_1 was upright or fused, S_3 was fused (Figs. 2, A and B, and 3B). An exception to this rule was observed in only 3 out of 50 electrocardiograms. It does not follow, however, that when S_3 is fused Q_1 is also fused. In 20 records out of 50, S_3 was fused while Q_1 was not.

According to Hurxthal (1933), in left axis deviation, Q_1 points down markedly and Q_3 shows a distinct upright deflection. In right axis deviation Q_3 points downwards (Q_1 being upright) and, if R_1 is slightly upwards, slurring of the origin of R will be found. One can reasonably assume this to be a

fusion of upright Q and R. Also he states that if the law of Einthoven can be applied to separate phases of QRS this will be helpful for correct identification of a deflection, as very often somatic tremor or other irregularities or abnormalities make it difficult to separate various components.

Paul White gives as limits for the R deflection in normal adults 5–35 mm. and in infants 5–10 mm. Pardee sets the lower limit at 7 mm. and by most authors smaller deflections than this are considered as low. Steuer (1933), taking 7 mm. as the lower limit reviews 50 cases with low voltage, all having had post-mortem examinations. All showed severe myocardial lesions due to coronary disease, tertiary syphilis, rheumatic heart disease, or nephro-sclerosis, or in a few cases miscellaneous causes such as acute or chronic infections, cancer, etc. Shipley and Hallaran record low voltage electrocardiograms under 7 mm. in three apparently normal subjects. In the Burnett and Taylor (1936) series, the results were : 55 cases, 17 mm. or over ; 44. 7 mm. or below ; 4, 3 mm. or below.

We accept the view that a deflection of R under 5 mm. in all leads (including lead IV) is rare and is a sign of serious myocardial damage. Below are recorded the values found in our 50 cases analysed according to leads :

TABLE V

SIZE OF R WAVE IN 50 CASES (PERCENTAGES)

Size of Deflection	Lead I	Lead II	Lead III	Lead IV
5–7 mm.	24	2	18	2
7–17 mm.	72	76	56	44
17–31 mm.	4	22	2	44
Mean value (mm.)	9·8	13·5	6·5	1·74

In 12 records the deflection of R in lead III was under 5 mm., 2 records being just under 2 mm.; in 6 it was between 3–4 mm., and in 4 between 4–5 mm. The maximum deflection of 31 mm. was found twice in lead IV. No slurring or notching was seen in our series of cases.

Duration of QRS. The earliest work on QRS duration was done by Lewis and Gilder (1912), who state that the normal duration must not be over 0·10 sec. We are reproducing here the values for QRS duration according to different investigators quoted from the paper of McGinn and Paul White (1933). Ferguson and O'Connor (1926) in 1812 young people report a duration of over 0·10 sec. only in 2 records ; Jensen, Smith, and Cartwright (1932), found a duration of 0·06–0·08 sec. in 50 patients. Seham (1921) reports the following values in children : birth to one year, 0·036 sec. ; one to five years, 0·05 sec. ; over five years, 0·07 sec. Lincoln and Nicolson (1928) give 0·06 in 222 normal school children. McGinn and Paul White, using the Lucas comparator described in detail by Lewis (1925), find the following figures : 50 males, average 0·083

(66 per cent. over 0·08 sec.) ; 50 females, average 0·072 (20 per cent. only over 0·08 sec.). The average for all cases and all ages was 0·078 sec. Eleven persons were tall, 10 of whom had a duration of QRS more than 0·083 sec. In 50 normal children under 12 years, 26 boys and 24 girls, the average QRS duration was 0·072 sec. The duration tends to be slightly longer in boys than in girls. Shipley and Hallaran (1936) found a smaller difference between the average QRS duration in males (0·087) and in females (0·085).

The values of the QRS interval found in our 50 normal cases differ to some extent from those reported by previous authors. In general the duration is shorter. The mean values were 0·06 sec. in the three limb leads and 0·05 sec. in lead IV. The shortest duration was 0·03 sec. and the longest 0·09 sec., both in lead III. Although lead IV shows the largest voltage, the QRS duration was the shortest in this lead. The measurements were made from Q or the beginning of the ascending spike of R to the beginning of S or in absence of S to the fusion of R and S. If Q and S deflection were " fused " with R or absent, the measurements were made at the level of the fused part on the base line. When R was diphasic the measurements were made from Q to the tip of the lower deflection of S.

It was thought that one of the reasons for the short duration of QRS was the fast rate found in most of our records, but no relationship between the duration of QRS and the duration of whole cycle could be established.

S-Wave. The variations of S are less frequent than those manifested by Q. There appears to be no definite relation between Q and S with regard to their form, nor is there at present any satisfactory explanation of the variations of the form of the S wave.

Amplitude. The S deflection is in general more conspicuous than Q and is greatest in lead IV, in contrast with Q which is smallest in this lead. The mean values that were found for S are shown in the first column following :

Lead	mm.	mm.
I	1·08	2·06
II	0·79	2·23
III	0·08	1·73
IV	3·28	—

The figures in the second column show the average values found by Lewis in normal adults. Burnett and Taylor (1936) report that S is deeper in children than in adults and that it decreases in size with age in all leads.

THE SECOND VENTRICULAR DEFLECTION OR T WAVE

We have analysed here separately the S–T segment (the interval between S to the beginning of T), the T wave itself, and the classical S–T duration. According to Lewis (1925, p. 119) there is always a definite relation between the direction of T and the direction of either Q or S, usually the latter. An upright T is always preceded by a downwards S, and if T is inverted S is usually upright, but if not, Q is upright. Since Lewis's work many investigations have been published

on the significance of the T wave and its relation to the initial deflections of the ventricular complex. According to Craib's (1930) conception there is no constant relationship between the direction of the T deflection and the direction of any deflection of the initial group, because the QRS deflection is recorded before there is any material movement of the myocardium, whereas the end deflection of T is recorded when there is a gross displacement of the myocardium. He held the view that the human electrocardiogram is composed of an initial quick deflection recorded before contraction and a prolonged end deflection recorded when the whole ventricular mass is in contraction. Theoretically each deflection is the result of multiple simultaneous contributions from all parts of the heart, and only the part of the summation that is in the same direction as the lead is recorded. Craib explains the electrical events recorded during ventricular activity by referring to his mathematical hypothesis of doublets, which is based on the view that currents flowing about active tissue must flow between anodes and cathodes localized at the affected part of the tissue.

S–T segment (S to beginning of T). Shipley and Hallaran (1936) point out that the level between QRS and T is influenced not only by the ventricular events but also by the so-called auricular T wave. We have measured in our records the deviation of the S–T segment from the P–R level. The S–T segment was most often raised in leads I and II, depressed in lead III, and slightly raised in lead IV. We cannot, however, draw a definite conclusion at present as we found difficulty in the identification of the auricular T effect.

Duration. On recording the duration of the S–T segment great difficulties are met with on account of the variation of form. The greatest value found was 0·24 sec. in lead III, and, as already stated, the segment was absent in a great number of records. The average values were as follows : 0·11 sec. in leads I and II, 0·13 sec. in lead III, and 0·10 sec. in lead IV.

The form and amplitude of the T wave. This varies with age. Burnett and Taylor (1936) in 167 healthy infants and children report well-defined T waves in leads I and II, and low voltage T waves in lead III in infants three weeks old. In children, T_1 is higher than the adult standard of 5 mm., T_2 reaches an amplitude of 8 mm., while T_3 is found to follow the adult type.

The authors describe also the susceptibility to external influences of T in childhood. In several records T_3 becomes inverted when the child changes from the recumbent to the sitting position. This appears to be due to some shift to the right, since mediastinal structures are very flexible in childhood. In adults it has a greater stability than in childhood, but this varies with the sex. In women, the T wave, especially in lead III, is less stable and shows a greater variation than in males. The round form T was more frequent in leads I and II, while the pointed form was more frequent in lead IV (62 per cent.).

The characteristic feature of T in some leads is the immediate take off from the R–S base with the rapid ascending peak and the abrupt drop. This type was more frequently met with in lead IV. We feel that this should not be interpreted as an absence of the S–T segment, but as a fusion between S–T and the ascending part of T. The evidence pointing in this direction is the existence of an increased time duration for T when the S–T segment is abrupt or fused.

This association was found 21 times in lead IV, 6 times in lead I, and 3 times in lead II.

Inversion of T was found most often in lead III (46 per cent.). The view of Lewis, that when T_3 is inverted, S or occasionally other deflections of QRS point in the opposite direction to T, is fully confirmed by our observations. Out of 23 records in which T_3 was inverted: S_3 was fused and upright in 12 records; upright in 2; and flat in 3 records; in the remaining 6 S_3 was downwards, with R inverted and Q upright in 4 records and with Q upright in 2 records.

As already stated the largest amplitude of T was found in lead IV, and an analysis of the deflection in all leads is reproduced in Table VI and in Fig. 4.
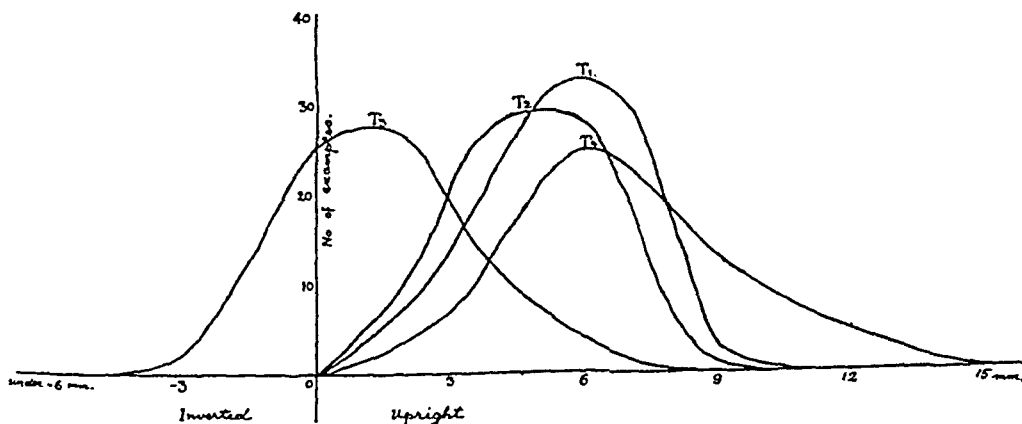

FIG. 4.—Frequency curves of the amplitude of ι in the four leads.

The average values of the amplitude are also as given in the table. It is interesting to note that the average value for T in lead I had a slightly larger value than in lead II in our records. This suggests two explanations:

1. There is a slight preponderance of the right over the left heart, in accordance with Lewis's bicardiogram hypothesis with regard to the summation of the events in both ventricles.

2. In young women the anatomical position of the heart and the axis of the direction of the change of potential are such, that in lead I the potential recorded for the T wave is slightly larger in certain cases than that recorded for the T wave in lead II.

This may explain also the large proportion of inversion (46 per cent.) and

TABLE VI

AMPLITUDE OF T IN 50 CASES (PERCENTAGES)

Range of amplitude in mm.	Lead I	Lead II	Lead III	Lead IV
−6 to −3	—	—	4	—
−3 to 0	—	—	50	—
0 to +3	28	42	38	14
+3 to +6	66	56	8	50
+6 to +9	6	2	—	26
+9 to +12	—	—	—	10
Average amplitude (mm.)	+3·23	+3·22	−0·74	+5·07

isoelectric T in lead III (30 per cent.). The S deflection shows also a larger average value in lead I than in lead II. In contrast with the T and S deflections the Q and R deflections show larger values for lead II than for lead I.

Duration of T. No relation was found between the amplitude of the T deflection and the duration. In Table VII below is reproduced the analysis of the T wave duration.

S–T Duration. The S–T segment and T wave added together form the S–T duration—the second part of the ventricular deflection. The range of values found in our records was 0·16–0·36 sec., the minimum being found in 3 records in lead III, and the maximum in 6 records in lead I, 3 records in lead II, 2 records in lead IV and 1 record in lead III. The average values were : lead I, 0·28 sec. ; lead II, 0·27 sec. ; lead III, 0·25 sec. ; and in lead IV, 0·28 sec.

TABLE VII

DURATION OF T IN 50 CASES (PERCENTAGES)

Range of duration in seconds	Lead I	Lead II	Lead III *	Lead IV
0·04–0·08	—	—	6	—
0·08–0·12	6	—	28	—
0·12–0·16	36	26	28	14
0·16–0·20	40	68	6	60
0·20–0·24	16	6	4	22
0·24–0·28	2	—	—	2
Mean value (seconds)	0·16	0·16	0·12	0·17

* T was isoelectric in 14 records in lead III, and in one record in lead IV, and therefore not measured.

The values found by us in 50 normal records are in general smaller than those given for adults in most books on electrocardiograms.

SUMMARY

An analysis of 50 normal electrocardiograms has been given. The form, amplitude, and duration of each deflection have been studied in the light of classical and recent investigations. The three standard leads and lead IV R, drawn according to the calculated mean values, are reproduced in Fig. 5. The
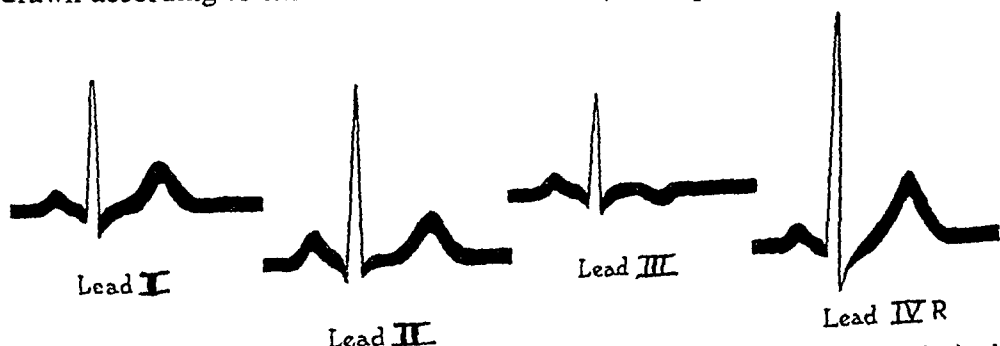

FIG. 5.—Standard four lead electrocardiogram drawn according to the mean values obtained in this series.

main part of the paper has been devoted to a detailed record and discussion of actual measurements of each component of the electrocardiogram.

In young women, each wave varies slightly from the values found by others for men and children ; both the voltage and duration appear to be intermediate, having in general lower values than in men and higher values than in children.

The classification of the components of the QRS deflection according to form has been a matter of some difficulty owing to the various views expressed by different authors. In describing Q and S it was found necessary to use the words inverted and fused, but we do not consider that the correct interpretation has yet been finally settled.

The form of R wave which we describe as diphasic is also a debated point. The other forms of R wave, however, were measured in accordance with the generally accepted view.

The S–T segment and S–T duration are studied separately in this paper. It was, however, difficult to ascertain the duration of the former on account of the frequency of the abrupt form which occurred mainly in lead IV.

The amplitude of T in lead I is a noticeable exception to our general conclusion that amplitudes have lower values in young women than in men. We regard as significant the frequent inversion of T in lead III.

Special attention has been paid to the findings in lead IV, and they have been compared with the other three leads.

Since we wrote this paper we have read the article by Chamberlain and Duncan Hay in this journal (1939). They made a study of 302 normal subjects, mainly in the third and fourth decades, and summarized the results in age groups covering seven decades. In general their values are similar to ours. We consider that the differences are accounted for by the fact that they investigated both sexes and a wider range of ages. In contrast with the 29 per cent. of inversion of T in lead III found by Chamberlain and Hay, we found 46 per cent. in our series of young women in their third decade.

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ELECTRICAL AXIS DEVIATION OF FIFTY NORMAL ELECTROCARDIOGRAMS

BY

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In a single muscle fibre the electrical axis—the line along which the greatest electromotive force is developed at a given instant while the muscle is excited—is in the same line as the fibre itself. In a somatic muscle the electrical axis is also in the same line as the muscle itself (Lewis, 1925). In the heart muscle, however, the excitation wave spreads from a normal or abnormal pace-maker and the electrical activity takes a complex path and spreads simultaneously in different directions as the heart fibres run at many different angles.

The diffuse course can be represented by an axis—a curve not lying in a single plane, but in space, as does the heart itself. For clinical use, however, to suit the limits of electrocardiography, the axis is represented by its projection on the anterior plane of the body to fit the Einthoven triangle or the standard leads. Finally the curve is further simplified by constructing the projection of this line on each lead or side of the triangle, and the angle which it makes with one of the sides is briefly used to designate the electrical axis of the electrocardiogram.

The electrical axis can be calculated trigonometrically or by a simple clinical method. In this paper are given the results of measuring the axis deviation in the records from 50 normal female medical students (see Hoskin and Jonescu, pages 33–46 of this number).

TRIGONOMETRICAL METHOD

The angle of deviation is calculated according to Einthoven's formula. The method is explained very clearly by Lewis (1925, p. 108). He points out that unless Einthoven's method is fully appreciated it is impossible to grasp the meaning and significance of these differences in the heights and directions of the deflections as they appear in the three body leads.

The size of angle varies according to the position of the arrow (heart electrical axis) in the triangle and its projection on the leads. Also the angle of the electrical axis varies slightly in relation to a given phase of the cardiac cycle. The direction of the resultant electrical axis of the heart lies within wider limits than does the anatomical axis in normal and abnormal hearts (Paul White, 1937).

The normal electrical axis lies between the degrees of 0 and 90. The axis deviations of our 50 normal electrocardiograms are shown in Fig. 1. If the

FIG. 1.—Distribution of axis deviation in 50 normal electrocardiograms.

angle has a minus value, that is above the horizontal line, or, in other words, if the arrow (electrical axis) in the Einthoven's triangle has shifted anti-clockwise, there is a so-called left axis deviation. If the angle has a value beyond 90° and the arrow (electrical axis) in the Einthoven's triangle has shifted clockwise, there is right axis deviation.

The frequency curve constructed from our analysis of the angles of axis deviation is reproduced in Fig. 2. The mean value for the angle of axis deviation was found to be +54·5°. It will be seen from Fig. 1 that in one record from a healthy athletic woman whose heart seemed normal (Case 31) there was an abnormal left axis deviation of −25°. Two records (Cases 13 and 38) showed a slight right axis deviation (+94° and +96°). The rest of the records show an angle within normal limits.

Paul White points out that it is more accurate to use the terms abnormal left and abnormal right axis deviation. Displacement upwards by a high

diaphragm so that the heart lies horizontally will give left axis deviation, even though the left ventricle remains normal. Similarly, a low diaphragm with a
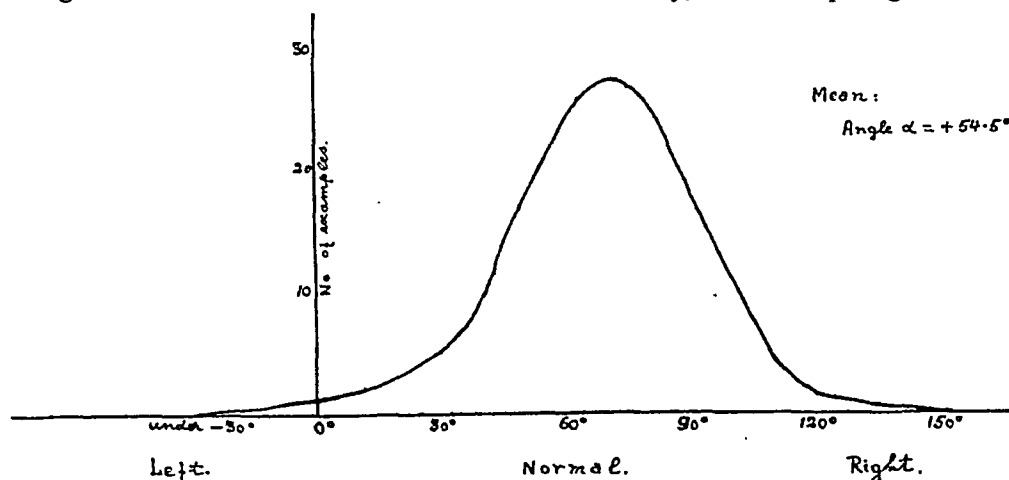

FIG. 2.—Angle of axis deviation : frequency curve.

vertical position of the heart will tend to give an abnormal right axis deviation, even though the right ventricle is small and the left ventricle may be preponderant. It is true, however, that a high degree of abnormal deviation is generally found with enlargement of the right or of the left ventricle ; though serious disease or enlargement of one or the other ventricle may be present with no evident abnormality of axis ; it is also true that when both ventricles are enlarged correspondingly, their effects tend to neutralize each other.

SIMPLE METHOD. INDEX OF AXIS DEVIATION

To estimate at a glance in clinical work the axis deviation, without the use of the trigonometrical method, the following formula is used :

$$Index = (R_1 + S_3) - (R_3 + S_1)$$

The index is derived by subtracting the sum of the amplitudes in millimetres of R in lead III and S in lead I from the sum of the amplitudes of R in lead I and S in lead III. According to Paul White, if the index measures over 30 mm., abnormal left axis deviation is present with a wide borderline of 20–30 mm. If the index measures under −15 mm., abnormal right axis deviation is present with a normal borderline of −10 to −15 mm. The analysis of index of axis deviation in our 50 normal subjects is reproduced in the following table :

INDEX OF AXIS DEVIATION IN '50 NORMAL CASES

	Range of Index in mm.	Percentage of Total
Right	−15 to −10	4
	−10 to −5	10
	−5 to 0	28
	0 to 5	24
	5 to 10	20
	10 to 15	6
	15 to 20	6
	20 to 25	0
Left	25 to 30	2

The mean value was +2·45 mm. One record (Case 31) showed left axis deviation that was almost abnormal (25–30 mm.) and three records (Cases 20, 21, and 45) showed slight or borderline left axis deviation (15–20 mm.). Two records (Cases 43 and 49) showed slight or borderline right axis deviation. The examination of the table and curves shows that in general both methods— the trigonometrical and the simple—agree, but that the trigonometrical is much more accurate. It will be seen that one electrocardiogram (Case 13) is shown by the trigonometrical method to be of right axis deviation, but by the simple method is found to be within normal range (index = −8). Also that the 5 records (2 of which were borderline right axis and 3 borderline left axis) are found to belong to the normal range of electrical axis deviation by the trigonometrical method.

Summary

The results of the measurements of the axis deviation of the electrocardiograms taken from 50 normal women students at the Royal Free Hospital have been measured and reported.

A comparison of the trigonometrical method and of a simple clinical method of calculation shows that there is a general agreement. The former is, of course, more accurate but the latter can be calculated quickly and easily and is accurate enough to be of practical use.

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THE RELATIVE VALUE OF CERTAIN DIGITALIS PREPARATIONS IN HEART FAILURE WITH AURICULAR FIBRILLATION

BY

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Digitalis is given universally in heart failure with auricular fibrillation, and to prevent the recurrence of failure it is the custom to continue it. Yet there is still doubt as to the best preparations to use and the dosage to maintain adequate digitalization. In this paper a clinical assay is attempted, based on a study of subjective and objective symptoms, and the results have been controlled by comparison with less potent remedies, both within and without the digitalis group. The place of digitalis in failure with normal rhythm has long been discussed, among others by Mackenzie (1911), Lian (1926), and Luten (1936), and more recently in this department by Gavey and Parkinson (1939). Here, however, I am dealing only with patients suffering from auricular fibrillation of rheumatic origin as proved by the coincidence of mitral stenosis.

Eighteen of the 25 patients accepted as suitable remain for the complete analysis : the other 7 failed to finish the entire schedule of the investigation ; one died at another hospital, two were admitted with pulmonary infarction, two left the district and were unable to attend, while two were omitted because the heart rhythm became normal even though they were under treatment with digitalis. The 18 patients consisted of 6 men and 12 women ; their ages varied from 25 to 59, with an average of 48 years. After routine clinical examination which included electrocardiography and radiocardioscopy they were chosen as comparable cases, in that they had in common three lesions—mitral stenosis, auricular fibrillation, and heart failure.

They were treated solely as out-patients and many of them followed their usual occupation. As a rule they attended hospital fortnightly, but occasionally they returned earlier on account of fresh symptoms. A different preparation was prescribed for each test period of 14 days, but never in the same rotation. At each attendance a record was made of the patient's activities and progress during the past test period, when any symptoms of heart failure or any toxic effects were noted, and a detailed clinical and graphic examination was carried out at intervals. After a brief rest at each interview, the pulse and heart rates were counted over half-minute periods and the mean of three

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consecutive readings was accepted. Although in this way there was a record for each patient of the *change in heart rate* following each medicine, it was clear that the drug could not be assessed on this criterion alone. For instance, the tincture of digitalis during a period following coramine might reduce the heart rate by 50 beats a minute, while if it followed a test period on digitalis leaf the heart rate might actually rise by 10 beats. This difficulty was partially avoided by prescribing the drugs in different sequence. It was found, however, that much greater reliance could be placed on a comparison of the *actual heart rate* at the end of each test period, for then the influence of the preceding drug was no longer operative. Further, the extent of heart failure, determined by symptoms and by clinical and radiological examination, tallied so closely with the heart rate that this came to be accepted as a reliable index of the state of digitalization for each patient. The heart rate following different preparations may be compared in the same patient, but the rate from the same preparation is not comparable in different patients. Depression of the R–T segment in the electrocardiogram proved that digitalis was in action and to some extent indicated its hold on the heart.

The following preparations were tested : digitalis leaf, tincture of digitalis, digoxin, digitaline (Nativelle), digitaline (Allen & Hanbury), digifoline, folinerin, strophanthin, and ouabaïne ; cardiazol and coramine were used as controls. The digitalis preparations were dispensed, in comparable doses in terms of biological assay, in some cases twice and in others three or even four times a day according to the judgment of each patient's need ; but the number of daily doses of any preparation was kept constant for each individual patient. The medicines were given for 14 days : with the one exception that cardiazol and coramine were given for 7 days only, because it was found unsafe to leave patients taking either of these drugs without medical supervision for as long as 14 days ; in reality it was digitalis they needed. Before giving an account of the results, the procedure adopted will now be instanced in one patient.

J. W., male, aged 45. Palpitation and breathlessness for several months, yet at work as a tailor until two weeks before admission when severe palpitation caused him to give it up. On examination : Rather stout. *Slight cyanosis and breathlessness, increased in recumbent position. Blood pressure normal.* Distension of veins of neck. Electrocardiogram, auricular fibrillation. Heart rate 164, pulse rate 124 a minute. Apex beat forcible and slightly displaced outwards. Harsh diastolic murmur in mitral area. Coarse and fine crepitations over both lung bases especially right. Liver not enlarged and no œdema of ankles. Urine trace of albumen ; daily output satisfactory. Radiogram, characteristic of mitral stenosis and heart failure. Satisfactory response to rest and digitalization during five weeks in hospital. Then referred to out-patient department and received into this series. Each medicine was given to the patient three times daily and his further progress is tabulated on the next page.

Date	Medicine during current test period	Dose given 3 times a day	Rate at end of test period		Patient's statement on progress
			Pulse	Heart	
5 January	Digitalis leaf	1½ grains	64	66	Well
19 ,,	Digitaline (Allen & Hanbury)	1/240 grain	68	76	Fair
2 February	Digitalis tincture	15 minims	66	76	Fair
16 ,,	Digoxin	0·25 mg.	76	80	Well
2 March	Strophanthin	1/100 grain	72	88	Well
16 ,,	Folinerin	0·1 mg.	80	92	Not well
30 ,,	Digifoline	1 tablet	70	74	Fair
13 April	Ouabaïne	1 mg.	70	94	Fair
20 ,,	Coramine	1 drachm	80	110	Not well
27 ,,	Cardiazol	1½ grains	88	104	Not well
4 May		,,	100	108	Not well
28 ,,	Digitalis leaf	,,	72	72	Better
25 June	,, ,,	,,	68	92	Fair
23 July	,, ,,	,,	64	68	Fair
6 August	Digitaline (Nativelle)	1/240 grain	56	56	Nausea + + Discontinued after 5 days
20 ,,	,,	1/600 grain	60	60	Better
3 September	Ouabaïne	5 mg.	77	76	Better
1 October	Digitalis leaf	1½ grains	80	80	Well

RESULTS OF OBSERVATIONS

The results for each preparation are first given, and then the several preparations are compared.   They are summarized in Tables I and II.

TABLE I

HEART RATE (PER MINUTE) IN 18 PATIENTS WITH AURICULAR FIBRILLATION AFTER TREATMENT

Patient					Preparation Used										
Case Number	Age	Sex	Weight (in lb.)	No. of Doses Daily	Digitalis leaf	Digitaline (Nativelle)	Digifoline	Digoxin	Tincture of Digitalis	Digitaline (A. and H.)	Folinerin	Ouabaïne	Strophanthin	Coramine	Cardiazol
1	55	F	106	2	87	88	88	86	96	86	92	82	94	100	108
2	25	F	104	3	65	72	72	70	80	66	96	80	104	86	110
3	56	F	134	3	60	72	72	80	108	80	96	116	92	94	116
4	41	F	98	4	74	84	75	92	78	85	80	134	150	124	128
5	49	F	149	3	98	80	88	98	92	86	110	120	108	134	106
6	45	M	200	3	68	60	74	80	76	76	92	76	88	110	104
7	44	M	184	3	80	84	78	80	110	88	76	84	110	96	98
8	65	F	114	2	64	78	100	98	84	98	90	100	92	152	140
9	48	M	116	2	52	50	56	56	58	64	46	66	74	78	78
10	53	M	147	3	104	115	116	120	88	118	140	108	130	128	135
11	51	M	135	3	70	46	62	66	90	68	104	80	84	114	96
12	58	F	182	2	74	74	92	76	62	84	106	116	106	98	112
13	46	F	84	2	52	62	72	64	72	84	100	124	130	100	130
14	53	F	98	2	80	80	98	88	76	100	72	110	146	90	122
15	37	F	104	3	74	80	78	94	106	94	88	94	90	96	126
16	54	F	154	2	66	102	100	92	70	86	92	88	98	112	120
17	42	F	185	2	84	88	70	77	96	96	98	92	104	104	150
18	59	M	147	2	94	102	120	106	126	110	136	128	120	154	136

Powdered digitalis leaf

Mackenzie (1911) chose to use either the tincture or the powdered leaf, and preference for the latter has been expressed by Wenckebach (1930), White (1931), Luten (1936), Fishberg (1937), and Gavey and Parkinson (1939).

Taking the cat unit as the minimal dose, per kilogram of cat-weight, proving lethal from slow intravenous injection of digitalis, it is estimated that 1 1/2 grains of well dried and undeteriorated powdered leaf contain a single cat unit. This dose was always given as a tablet composed of pulvis digitalis folia (B.P) which is comparable with that in the United States Pharmacopœia (1936). Campbell (1938) thinks that in clinical practice digitalis leaves are stronger than when estimated from animal experiments and on the basis of clinical observations advises that tab. dig. fol. gr. i., rather than gr. 11/2, can be taken as a close equivalent of 15 minims of the tincture.

The heart rate at the end of the test periods varied from 54 to 104 a minute with an average of 75 for the 18 patients. This proved to be the lowest level obtained from any preparation tried. Similarly the powdered leaf proved its superiority when its value was based on the reduction of the rate from the preceding period. A reduction was effected in 17 patients with an average fall of 19 beats a minute, the maximum fall being 46.

Clinical improvement was invariably produced, and nausea was only reported once.

Tincture of digitalis

Bramwell (1932) prefers standardized tincture of digitalis to any other preparation. Lewis (1934) states that as a routine the tincture should be used.

Since 15 minims of the 10 per cent. tincture represent one cat unit of digitalis, it equals 1 1/2 grains of the powdered leaf and therefore it was prescribed in this dose.

The heart rate at the end of the test periods varied from 58 to 126 with an average of 87 beats a minute. When the change in the rate from the preceding period was studied, it was found lowered in 8, increased in 8, and unchanged in 2 patients. The greatest fall was 64 and the greatest rise 32 beats a minute while the average for all patients was a fall of 3.

Clinical improvement was noted in every case. Nausea occurred in 3 patients.

Digitaline (Nativelle)

This is a glycoside derived from the leaves of the foxglove, Digitalis purpurea, and is said to be a chemical entity, constant in its physical characters and chemical reactions, and not requiring physiological standardization. It is usually dispensed as white and pink granules, the white granule containing 1/240 grain (0·25 mg.) and the pink granule 1/600 grain (0·1 mg.). Mackenzie (1911) compared the clinical effects of the tincture of digitalis with Nativelle digitaline, and found that 1/240 grain (white granule) of digitaline was equal to

15 minims of the tincture. Campbell (1938), from clinical observations, concluded that 1/600 grain (pink granule) of Nativelle digitaline was equivalent to 15 minims of the tincture of digitalis. Stroud and Vander Veer (1937) reported on five preparations of digitalis observed over a period of six years. On comparing verodigen, a gitalin glycoside of digitalis, with digitaline (Nativelle) they found that 1/600 grain of the latter produced the same clinical effects as 1/240 grain of the former.

In the present series digitaline (Nativelle) was first tried in a dose of 1/240 grain (white granule). Without exception it produced severe nausea and vomiting between the second and fifth day and had to be discontinued. Most of these patients reported prematurely to hospital, when the heart rate was found to be very slow ; though a few returned at the end of the prescribed test period, when the rate was more rapid from the lack of digitalis therapy for eight or more days. Later it was decided always to use the pink granule containing 1/600 grain.

The heart rate at the end of the test periods varied from 46 to 115 a minute with an average of 79. When its value was based on the reduction of the rate from the preceding period, it was found lowered in 15 patients, raised in 2, and unchanged in another. The greatest fall was 50 and the greatest rise 10 beats a minute, while the average for all the patients was a fall of 12.

Clinical improvement was noted in every patient, and toxic symptoms were never reported from the pink granule (1/600 grain).

Digitaline (Allen & Hanbury)

This preparation, said to consist of the active principle of the foxglove, is supplied as pink and white granules similar in appearance and dosage to those of Nativelle digitaline. For this investigation only the white granule of 1/240 grain was used.

After its administration for test periods of 14 days the heart rate varied from 64 to 118 a minute, with an average of 87. When its value was judged by the reduction of the heart rate from the preceding period, it was lowered in 7 patients, raised in 8, and unchanged in 3. The greatest fall was 22 and the greatest rise 24 beats a minute, while the average was a rise of 3.

Efficient digitalization was obtained in every patient, and toxic effects were never seen.

Digifoline

This standardized preparation made by Ciba is said to contain all the therapeutically active glycosides of digitalis leaf. Each tablet is claimed to be equivalent to 1 1/2 grains (0·1 g.) of the standard digitalis leaf so this dose was used.

At the end of the test periods the heart rate varied from 56 to 115 with an average of 84 beats a minute for all the patients. When it was evaluated by the reduction of the rate from the preceding period, it was lowered in 15 patients

raised in 2, and unchanged in another. The greatest fall was 42, the greatest rise 10, and the average was a fall of 15 beats a minute.

Digifoline never occasioned toxic symptoms and efficient digitalization was established in every patient.

Digoxin

Digoxin, a crystallized glycoside isolated from the leaf of *Digitalis lanata*, is prepared by Burroughs Wellcome and is said not to require biological standardization. Each tablet contains 0·25 mg.

The heart rate at the end of the test periods varied from 56 to 120, with an average of 85 beats a minute for all patients. When its efficiency was calculated from the reduction of the rate from the preceding period, it was found to be lowered in 10 patients, raised in 7, and unchanged in another. The greatest fall was 36 and the greatest rise 14, while the average for all patients was a fall of 8 beats a minute.

Clinical improvement was always obtained, but anorexia was noted once.

Folinerin

Folinerin, prepared by Schering, is a crystalline glycoside obtained from the eaf of *Nerium oleander*, and a digitalis-like action is claimed for it. Each tablet contains 0·1 mg.

The heart rate at the end of the test periods varied from 46 to 140, with an average of 95 beats a minute. When its value was judged by the reduction of the rate from the preceding period, it was found to have been raised in 10, lowered in 6, and was unchanged in 2 patients. The greatest rise was 38 and the greatest fall 32, while the average change was a rise of 3 beats a minute.

No toxic symptoms were observed, but noticeable clinical improvement was only recorded in 2 patients.

Strophanthin

Strophanthin, a glycoside isolated from the seed of *Strophanthus kombé*, is seldom used in this country for the continuous treatment of heart failure. Tablets, each containing 1/100 grain, were used.

The heart rate at the end of the test periods varied from 74 to 150 beats a minute, with an average of 106 for all the patients. When the efficacy of the drug was judged by the change of rate from the preceding period, a rise had taken place in 15 patients, a fall in 2, and there was no change in 1 patient. The greatest rise was 36 beats a minute and the greatest fall 6, while the average for all patients was a rise of 13.

In 5 patients the symptoms of heart failure increased during the test period on strophanthin, and none showed any clinical improvement.

Ouabaïne

Ouabaïne, a strophanthin glycoside isolated from the *Strophanthus gratus*, has a different formula from ordinary strophanthin. Tablets containing 5 mg. (1/12 grain) were used.

The heart rate at the end of the test periods varied from 66 to 134 beats a minute, with an average of 100 for the 18 patients.   When its value was judged by the change of rate from the preceding test period, a rise was found to have taken place in every patient ; the greatest rise was 64 beats a minute and the average 22.

Five patients complained of headache, depression, and breathlessness. Clinical improvement was not once recorded.

The results obtained with the different preparations are summarized in Table II.

TABLE II

THE CHANGE IN HEART RATE IN 18 PATIENTS WITH AURICULAR FIBRILLATION FOLLOWING TREATMENT

Medicine prescribed	Average Heart Rate for 18 patients at end of test periods	Number of Patients where the Heart Rate was			Net average of Change of Heart Rate
		Lowered	Unchanged	Raised	
Digitalis leaf	75	17 (20)*	0	1 (2)*	−19
Digitaline (Nativelle)	79	15 (15)	1	2 (8)	−12
Digifoline	84	15 (19)	1	2 (6)	−15
Digoxin	85	10 (19)	1	7 (6)	−8
Tincture of digitalis	87	8 (24)	2	8 (16)	−3
Digitaline (Allen&Hanbury)	87	7 (6)	3	8 (14)	+3
Folinerin	95	6 (14)	2	10 (14)	+3
Ouabaïne	100	0 —	1	17 (23)	+22
Strophanthin	106	2 (4)	1	15 (16)	+13
Coramine	109	0 —	2	16 (26)	+21
Cardiazol	117	1 (8)	2	15 (23)	+19

* The figures in brackets show the average reduction or rise, in beats per minute.

Cardiazol

Cardiazol or metrazol has a formula related to camphor, and by some it has been acclaimed as a " heart stimulant " that reduces the heart rate and increases the venous flow, coronary flow, and the cardiac output.   Cardiazol was tested, not in the belief that it possesses a digitalis-like action, but rather as a comparison with the other drugs.   It was given orally as tablets containing 1 1/2 grains (0·1 g.), but the test period of 14 days was reduced to 7 for it became evident after trial that it was unsafe to withhold digitalis from patients in this series for longer than a week.

The heart rate at the end of the test periods varied from 78 to 150 beats a minute, with an average of 117 for the series.   When its value was estimated from the change of rate from the preceding period, there was a rise in 16 patients. The greatest rise was 48 beats a minute and the average 19.

Breathlessness, palpitation, weakness, and headache, appeared in 9 patients, and clinical improvement was not once recorded.

Coramine

Coramine, reputed to be a " cardiac stimulant," is widely used. It was given orally to each patient in this series in the optimum dose of 30 minims (2 c.c.) ; but, like cardiazol, it was included more as a control than for its alleged value. As with cardiazol, it was found unsafe to allow patients taking it to be without medical supervision for more than 7 days, by which time the lack of digitalis had become evident.

The heart rate at the end of the shorter test periods varied from 78 to 154 beats a minute, with an average of 109 for all patients. When its value was judged by the change of the rate from the preceding period, a rise was recorded in every case. The greatest rise was 62 beats a minute and the average 21.

Headache was distressing in 7 patients and clinical improvement was not once recorded. In 15 patients the symptoms of heart failure reappeared during its administration.

The shorter test period adopted for cardiazol and coramine has to be taken into account when comparing their influence on the heart rate and their clinical effects with those of digitalis preparations, because the recorded rates would be much higher after the standard and longer test period and the symptoms of heart failure correspondingly greater.

DISCUSSION OF RESULTS

The scarcity of controlled observations on the clinical effects of various digitalis preparations prompted this inquiry into their relative value. Mackenzie (1911) compared the effects of the tincture with Nativelle digitaline and a pill containing powdered digitalis leaf, squills, and mercury. He watched for the first sign of a digitalis reaction and then noted the quantity of the drug which had induced it. In 1925 Cushny deprecated the fact that even though many preparations were employed, little had been done in the way of accurate comparison of their effects in man. Luten (1936) stated that on the basis of both animal experiments and clinical experience there was no valid reason for preferring one particular digitalis preparation to another on the grounds of some alleged selectivity of action on the heart.

The right choice of a preparation and of dosage will not be decided from experiment in animals, but from such comparison in patients as is attempted in the present investigation. When judged by amelioration of failure symptoms, freedom from toxic effects, and decrease in the heart rate, 6 of the 11 preparations tried proved satisfactory. Arranged in the order of therapeutic efficiency when used in customary doses, they were : powdered digitalis leaf, digitaline (Nativelle), digifoline, digoxin, tincture of digitalis, and digitaline (Allen & Hanbury). Three preparations, folinerin, ouabaïne, and strophanthin, never produced satisfactory digitalization, and their routine use in patients with heart failure is unjustified. As to cardiazol and coramine, which served to control the observations on the other drugs tried, it was not expected that either would reduce the heart rate or master the symptoms of failure, but it was

surprising to find that, apart from not benefiting a single patient, they induced ill effects so frequently. It is clear that neither cardiazol nor coramine have any place in the *continuous* treatment of heart failure. The comparison is well shown in Fig. 1, which also indicates the cost of treatment and shows that the more effective preparations are not the more expensive ones.
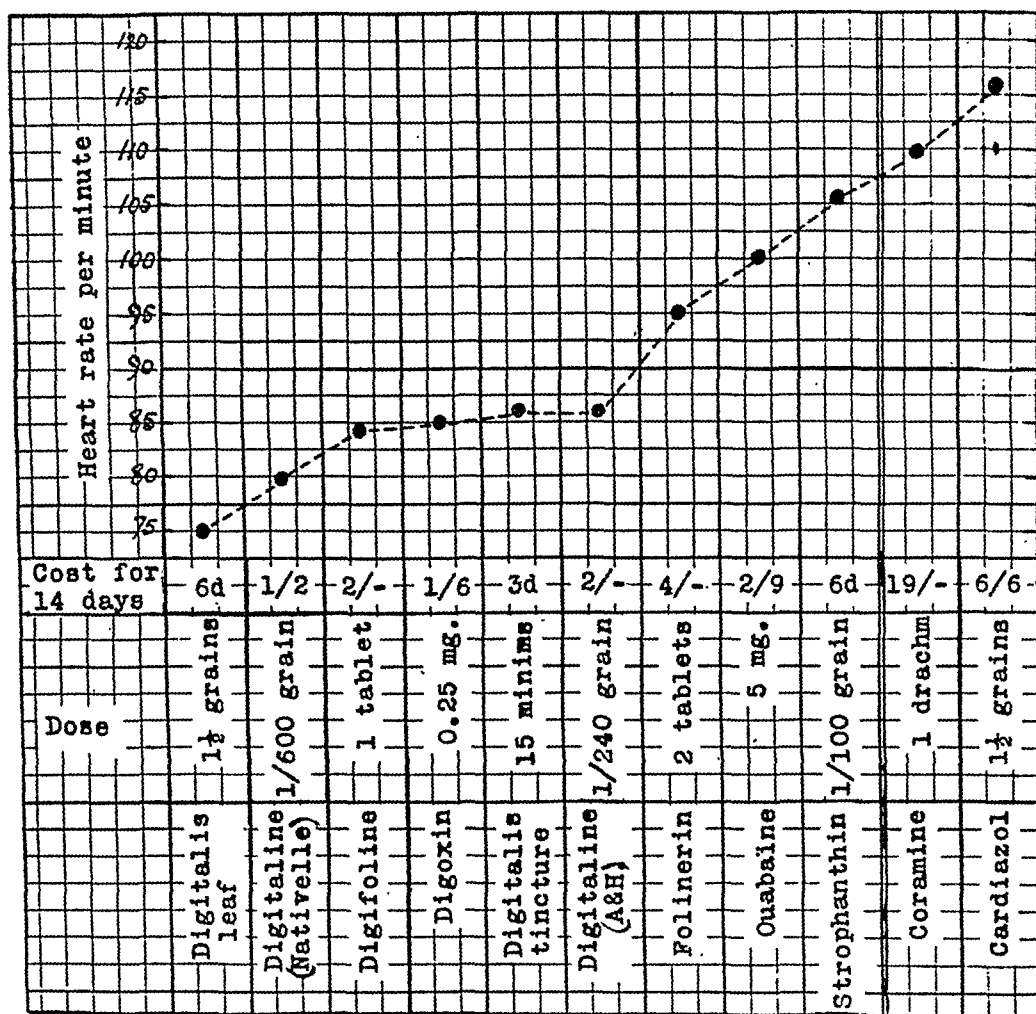

FIG. 1.—The effect of drugs on the heart rate in 18 patients with auricular fibrillation. An average rate of 90 has been accepted as the uppermost level of satisfactory digitalization for this series. The cost of each drug is quoted, for hospital patients receiving it three times a day for a fortnight. Drugs to the left of the upright double line were given over periods of 14 days; those to the right, over periods of 7 days.

The dosage of digitalis for ensuring adequate digitalization has long been in dispute, but most authorities think that it must be determined separately in each patient. Withering's (1785) opinion was that digitalis should be continued until it acted on the kidneys, stomach, pulse, or bowels, when it should be stopped. Mackenzie (1911) said that patients instructed on the symptoms indicating a sufficiency of the drug could generally help thereby to decide the dosage that suited them. Eggleston (1915 and 1920) devised a formula for

estimating the amount of digitalis required to produce a state of digitalization, founded on the body weight and the amount of digitalis preparation to one cat unit.

In a clinical investigation of digitalis action, Lyon and Gilchrist (1927) found wide variation in the effects of uniform doses as calculated from the body weight. Baker and Bloom (1936) found that the experimental cat unit was not a reliable index of the proper clinical dosage, nor could this be determined in patients by means of Eggleston's formula. Luten (1936) said that the optimum dose of digitalis, whether for the induction of its effects or for its maintenance, should be judged individually ; and he urged that no patient should receive an arbitrary dose in an attempt to bring about some anticipated effect, but rather that the effect produced must always determine the dosage.

This investigation has confirmed the view that the dosage of digitalis cannot be predicted for each patient and that it can only be settled after clinical trial. Evidence is produced that it is not possible to calculate the appropriate clinical dose of any digitalis preparation from biological standardization, nor yet from the patient's body weight. Thus digitalization of a patient of heavy weight was sometimes maintained by small doses of digitalis, while that of a patient of light weight was often only reached by larger doses (see Table I).

Throughout the investigation the *single* dose of each preparation was kept constant, as was the *daily* dose for an individual patient, but all did not receive an identical amount, and the decision on this had to be taken in each case after a preliminary clinical trial. Thus for powdered digitalis leaf a dose of 1 1/2 grains was always prescribed, but the daily dose was twice a day in 9 patients, three times a day in 8, and four times a day in 1 patient.

The fallacy of deducing the value of a digitalis preparation from a comparison of its effect upon heart rate in different patients became more apparent as the investigation proceeded. True evaluation must therefore depend on a *comparison* of the heart rate after treatment with *different* preparations in the *same* patient. In fact, the heart rate during successful digitalization differs widely among patients with auricular fibrillation (see Table I). In one a satisfactory rate was 115, but in another 52 beat a minute, directing our greater attention to the abatement of failure symptoms and the reduction of the pulse deficit as the indications of improvement.

In this country four manufacturing chemists supply *digitaline* granules that are similar in colour and dosage to those prepared by Nativelle. Although the dosage is the same, the therapeutic effect may differ greatly ; and certainly of the two brands tested in this investigation, Nativelle digitaline produced digitalis benefit that was twice as great as that gained from Allen and Hanbury's digitaline. One must, therefore, know which product is being used, so that an appropriate amount may be ordered.

CONCLUSIONS

The effects of six preparations of digitalis and of three others with a digitalis-like action were watched in eighteen comparable cases of auricular

fibrillation with mitral stenosis and heart failure.   Each preparation was tried in every patient, and its value was assessed at the end of test periods of fourteen days, with due regard to the heart rate, pulse deficit, failure symptoms, toxic effects, and electrocardiographic changes.   The observations were controlled by introducing test periods during which digitalis was not given in any form and cardiazol or coramine were the only drugs prescribed.   The following conclusions were reached :

1. Efficient digitalization was always induced and maintained by powdered digitalis leaf, digitaline (Nativelle), digifoline, digoxin, tincture of digitalis, and digitaline (Allen & Hanbury), mentioned in the order of their therapeutic activity in customary doses and from a practical standpoint.

2. Powdered digitalis leaf proved to be the best preparation for maintaining equable digitalization.   It was also one of the cheaper preparations.

3. Digitaline (Nativelle) in a dose of 1/600 grain (pink granule) showed greater digitalis effect than digitaline (Allen & Hanbury) in a dose of 1/240 grain (white granule).   Digitaline (Nativelle) in a dose of 1/240 grain (white granule) proved too potent for continuous use.

4. Folinerin, ouabaïne, and strophanthin (orally) failed to produce adequate digitalization and their routine use in heart failure is not justified.

5. Symptoms of heart failure developed in every patient when either cardiazol or coramine was prescribed without digitalis.

6. The actual heart rate was found to be an unreliable index of successful digitalization ; thus for one patient it was 115 during a period of maintained clinical improvement and for another 52 beats a minute.   The heart rate gains the greatest significance when the digitalis effect of different preparations is estimated in the same patient.   Freedom from symptoms and signs of heart failure served best to indicate successful digitalization.

7. It proved a good custom to adopt a standard dose for each digitalis preparation and to vary only the total daily dosage.   Thus with powdered digitalis leaf, the single dose of 1 1/2 grains was always employed, but this was given either twice, three times, or four times a day, according to need.

8. The optimal dose of digitalis could not be predicted with any accuracy, and it had to be sought by trial and error, thus implying a therapeutic study in every patient.

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CONGENITAL ANEURYSMS OF ALL THREE SINUSES OF VALSALVA

BY

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Aneurysm of a single sinus of Valsalva, though rare, is not so rare as to justify a detailed description of a single case. For it is recognized that both syphilis and ulcerative endocarditis may produce aneurysms or aneurysmal dilatations of the sinuses, and the causation is not obscure. In a small number of such aneurysms no evidence of these two causes has been found and it has been suggested that they may be congenital ; at least eleven such cases have been recorded, mostly involving the right (or anterior) sinus only.

But aneurysms of all three sinuses of Valsalva are extremely rare. I have been able to find records of only three such cases, and comparison of these with the one here reported suggests that it presents a condition that has not been recorded previously.

CLINICAL NOTES OF THE TERMINAL ILLNESS

The patient was a young man, aged 25, well built and of healthy appearance. His family doctor had for some time known that he had an enlarged heart and a systolic apical murmur, but these signs had been discovered in a routine examination and he had never complained of any symptoms that could be attributed to the heart. He was accustomed to cycle in all weathers and played golf without breathlessness or fatigue.

About a month before his admission to hospital, when pushing a lawn-mower on his holiday, he collapsed with pain in the chest, shortness of breath, and a feeling of great weakness. He stayed in bed six days, but on getting up had a similar attack and was again in bed a few days. On returning to his office work he felt as well as ever for a few days.

July 12, 1938.—He awoke early in the morning one hour after falling asleep, with a feeling of heat, of pain referred to the region of the xiphoid, of cough, and of shortness of breath. His doctor found an irregular pulse of over 100, a temperature of 101° F., and crackles over the apex of the right lung.

The same evening he was admitted to Sir Patrick Dun's Hospital under the author's care. His general condition was little changed. The pain was referred to the upper abdomen a little to the left of the midline. The apex beat was felt in the left anterior axillary line and there was a systolic murmur

heard best at the apex. The heart rate was 50 and slightly irregular, and the blood pressure was 130/60. The liver was enlarged and palpable one or two inches below the costal margin. The spleen was not to be felt. The temperature was still 101° and the respiration rate 46.

Both pleural spaces were explored under local anæsthesia, no fluid being found. The pericardial sac also was punctured in the region of the left ventricle. Digoxin, 0·5 mg. intravenously, produced no change in the heart rate. No other drug of the digitalis group was administered, then or previously. It is hardly likely that this single dose of digoxin can have played any part in producing the disturbances of heart rhythm subsequently recorded. The tentative diagnosis at this stage was an acute infective process, but next day it was recognized as cardiac failure due to a gross disturbance of rhythm.

July 13.—The patient slept lightly, thanks to an injection of 1/8 grain of morphine, and was much the same. A blood culture proved to be sterile. The Wassermann reaction was negative. Hæmoglobin, 70 per cent.; red cells, 4,800,000; white cells, 17,000. The heart rate was 40 in the morning and 35 by the evening.

There was total heart block (A, 100; V, 40 to 50). The ventricular complexes were prolonged beyond 0·1 sec. and there were many right ventricular extrasystoles (Fig. 1A).

July 14.—There was a marked change for the worse, the patient appearing

A   B
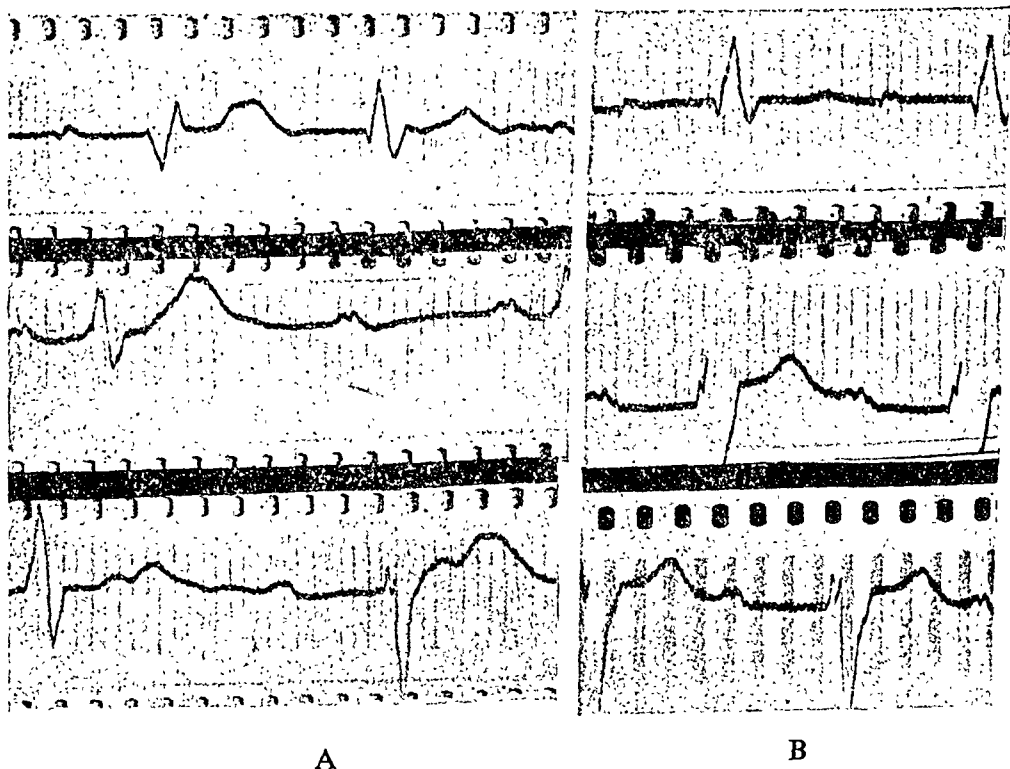
FIG. 1.

(A) July 13. Total heart block. Auricular rate 100, ventricular rate 40–50.
(B) July 15. Regular sinus rhythm. Rate 68. Left ventricular preponderance.

on the verge of death. Adrenaline was given for the first time, with good effect. After 2·5 mg. the rate rose from 25 to 75, and the blood pressure from 125/50 to 135/75. After two and a half hours the rate had fallen to 36, and 1·0 mg. of adrenaline was given, again with good effect. After a third injection of 1·0 mg. adrenaline, when the rate had again fallen to 32, it rose only to 52, but was maintained at 48.

A dramatic change for the better took place that evening, probably owing to a return of sinus rhythm. At 9 the heart rate was 52, at 9.40 it was 124, and at 10 it was 114; the patient said he was very much better and it almost seemed that the illness was over.

July 15.—After a good night with the help of 1/8 grain of morphine, he still felt very well. The heart rate was 79 and the pulse strikingly dicrotic, this being so pronounced that it was hard to tell by palpating the radial artery whether the heart rate was 80 or 160. The blood pressure readings of this dicrotic pulse were: systolic a little over 120 and diastolic between 70 and 75. It is interesting to speculate on the possibility of a connexion between the gross abnormality subsequently found in the patient's heart and the presence of this very remarkable dicrotic pulse on the only day when we had an opportunity of observing the patient with the heart rhythm normal.

The liver was still enlarged. The apex beat was diffuse and reached two inches outside the nipple line in the 5th and 6th spaces. There was a snappy first sound and faint (non-crescendo) pre-systolic and systolic murmurs, with no thrill. There was no œdema. As there were no physical signs of disease in the lungs and the presence of a cardiac lesion of radiological interest was not suspected, radioscopy was postponed to avoid tiring the patient; but next day he was too weak, so the opportunity of securing an X-ray picture of a very rare abnormality was missed.

The heart rate did not vary throughout the day and the patient's condition remained good. There was regular sinus rhythm, with a P-R interval of 0·3 sec. The QRS complexes were more than 0·1 sec. and resembled the extra-systoles of the first electrocardiogram (Fig. 1B).

July 16.—The patient had not had a good night and was worse. During the night the pulse rate had been variable and settled at a lower level—74, 52. 40, 52, 72, and at 9.30 between 48 and 52, and slightly irregular. At 11 a.m, 1·0 mg. of adrenaline produced a rise from 36 to 54 and also a rise of blood pressure from 110/40 to 140/60.

Fig. 2A, 105 minutes after the adrenaline, showed total heart block. The auricular rate was now 210, and the P waves differed greatly from those in Fig. 1. The ventricular complexes now showed left ventricular preponder-ance, and T₃ was deeply inverted. Presumably the rhythm was auricular flutter or auricular paroxysmal tachycardia.

During the remainder of this day adrenaline was given on several occasions and relieved the patient considerably, but his condition at the best was far more grave than on the previous day.

July 17.—The patient was still gravely ill. During the night adrenaline was given twice, when the rate dropped below 40.

Total block was present at noon, 9 and 14 hours after administration of adrenaline and of ephedrine respectively. The auricular rate was 210. Flattening of all the T waves as compared with the previous day was noted (Fig. 2B).
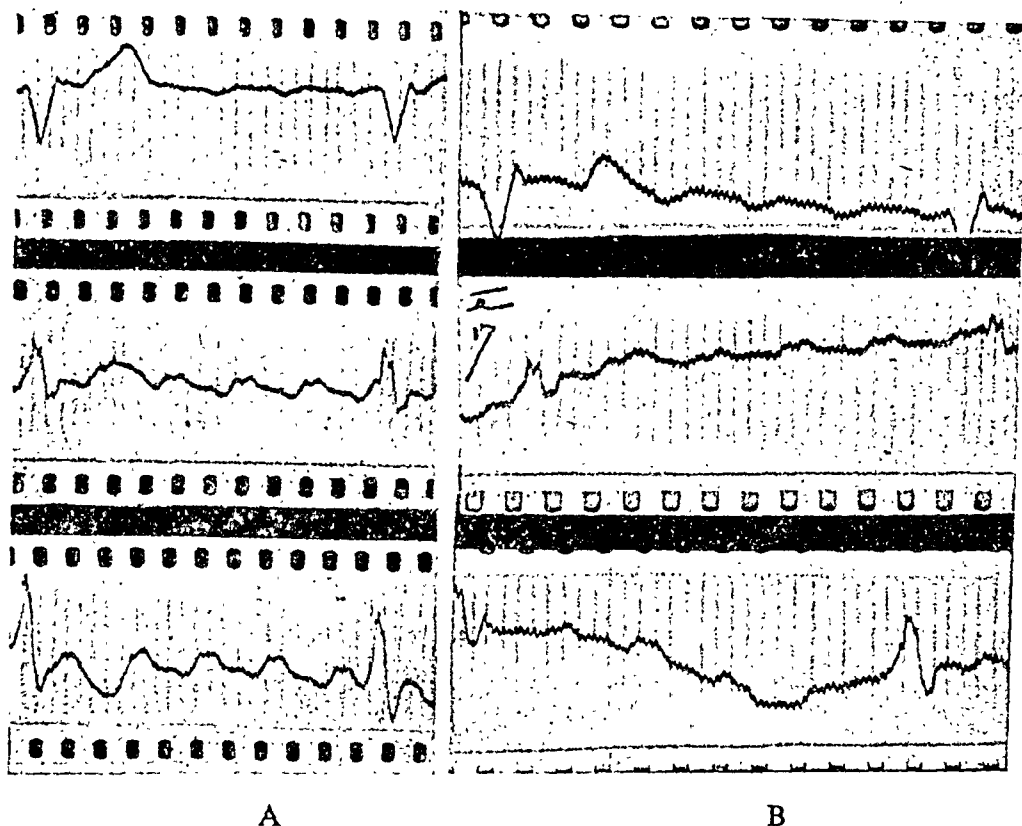

A   B

FIG. 2.—Complete heart block. Auricular rate 210.

(A) July 16. 105 minutes after adrenaline. P waves greatly differing from those of Fig. 1A. Presumably auricular flutter or auricular paroxysmal tachycardia.
(B) July 17. No adrenaline in preceding 9 hours. Note flattening of all T waves in comparison with (A).

During the day the rate varied from 38 to 52 and no ephedrine or adrenaline was given. At 6 p.m. the rate was 40 and 1/2 grain of ephedrine was given. Ten minutes later the rate was 114 and the patient was feeling better. Nevertheless he was still gravely ill.

July 18.—During the previous night the rate had varied between 120 and 148, and no drugs had been given except 1/8 grain of morphine early in the night.

Fig. 3A, taken at 10.30, showed a regular ventricular rate of 138. The new change of the QRS complexes should be noted, P_1 being still inverted. The rhythm seemed to be 2 : 1 heart block in auricular flutter or tachycardia.

At 5 p.m. the rate was still fast, 128, but four hours later it was 62. Ephedrine, 1/4 grain, was then given orally, a rise to 74 following. Fig. 3B, taken soon after, showed what appeared to be an auricular tachycardia of the same rate as before, now with a 4 : 1 ventricular response.

July 19.—The patient's condition was not such as to give rise to acute

anxiety till 9 a.m., when he became dyspnœic. The rate was then 46, a rate which had been noted frequently throughout the night without concomitant dyspnœa. Ephedrine and adrenaline relieved the dyspnœa slightly, although

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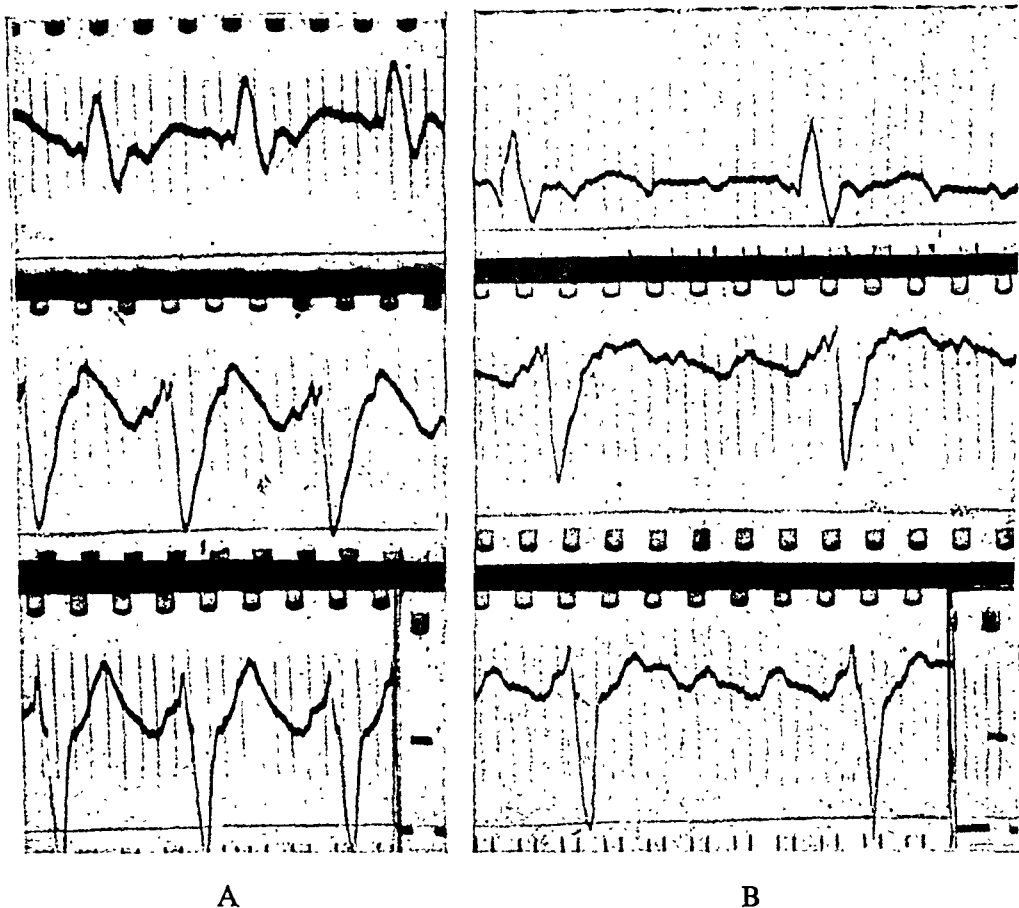
FIG. 3.

(A) July 18. No drugs except morphine in preceding 30 hours. Regular ventricular rate of 138. P_1 still inverted. Note new change of QRS complexes. Query, 2 : 1 heart block in auricular tachycardia or flutter.

(B) July 18. Just after pulse had been raised from about 62 to about 74 by ephedrine. Apparently auricular tachycardia of same rate as (A), now with a 4 : 1 ventricular response.

the rate increased only from 40 to 48. At 11 he was still dyspnœic ; the heart rate was 50, very irregular and hard to count even by auscultation. Repeated injections of adrenaline and ephedrine were given without benefit. At 2.50 p.m. the rate was recorded for the last time as 32, and at 3 p.m. the patient died.

Autopsy

A complete autopsy was not made, but the thoracic viscera were removed. The lungs showed congestion only. The heart and pericardium were removed intact and placed in preservative. Some time later the pericardium was

opened and an abnormal prominence to the left of the pulmonary artery was noted, but the cavities of the heart were not opened until the main trunks of the coronary arteries had been dissected out throughout their superficial course and found to be normal.

When the cavities of the heart were opened the three dilated pockets or aneurysms of the sinuses of Valsalva were at once apparent. They were filled with some recent soft blood-clot. There was also a considerable amount of old brown blood-clot, fairly firmly adherent to the inner walls of the sinuses, and this was picked off with a dissecting forceps.

NOMENCLATURE OF THE AORTIC CUSPS

When the left ventricle is opened out, the use of such terms as " right," " left," " anterior," and " posterior " as descriptions of the aortic cusps and the sinuses that lie behind them may be confusing. The cusps are most readily identified by the mouths of the coronary arteries and the simplest method of description would be that of right coronary, left coronary, and non-coronary cusps. For that reason we have used a terminology that corresponds closely to this and for the sake of convenience we append the following glossary :

The right aortic cusp is the cusp behind which the right coronary artery arises. It is also known as the anterior aortic cusp (British Revision, 1933).

The left aortic cusp is the cusp behind which the left coronary artery arises. It is also known as the left posterior aortic cusp (B.R.).

The posterior aortic cusp is the cusp behind which no coronary artery arises. It is also known as the right or right posterior aortic cusp (B.R.)

DESCRIPTION OF THE HEART

The heart was large, weighing 750 grammes. After it had been freely opened it was found to measure externally 14·5 cm. from base to apex by 13·2 cm. from side to side.

The pericardium was normal in appearance except for a small patch of fibrinous pericarditis at the apex, the result of the exploratory puncture made seven days before death.

The coronary arteries had been dissected out throughout their course outside the heart muscle before the cavities of the heart were opened. They could be seen lying free from overlying connective tissue and were normal in appearance.

The only striking abnormality to be seen from outside was the large prominence (well shown in Fig. 4) lying to the left of the pulmonary artery.

The wall of the right auricle was 0·3 cm. thick, and of the left 0·3 cm. thick. The wall of the right ventricle was 0·5 cm. thick, and that of the left from 1·5 to 2·0 cm. at its thickest.

The cavities of the auricles and of the right ventricle were normal, except for the bulges to be seen on the ventricular walls of the auricles and the septal

wall of the right ventricle. There was no defect of the inter-auricular septum ; no evidence of endocarditis, past or recent, on either walls or valves ; and no thinning of the walls at any of the points where they were deformed by the bulges. The pulmonary and tricuspid valves were normal ; also the cusps of the mitral valve ; but the mitral opening, 9·5 cm. in circumference, was considerably stretched and probably incompetent during life.

Inspection of the cavity of the left ventricle showed that each sinus of Valsalva was expanded to a large aneurysm or pouch. A detailed description

FIG. 4.—External view of the heart. Cavities had already been incised, but the outline was restored so far as possible. Arch of the aorta seen at the top. Below it the pulmonary artery. Beside it part of the left ventricle, showing protrusion of the aneurysm of the left sinus (slightly overlapped by the left auricular appendage). The root of the aorta is not shown.

of each aneurysm will be given, but a brief general description should make it easier to understand the anomaly.

The cavity of the left ventricle is described by anatomists as consisting of two parts : the main body of the ventricle with trabeculated walls ; and the aortic vestibule, that part of the cavity lying immediately below the aortic cusps, with smooth non-trabeculated walls. Normally this aortic vestibule forms a small part of the cavity, being a shallow irregular collar less than 1 cm. in depth. In the hypertrophied left ventricle this collar may be deeper.

The abnormality found in our specimen consists in this, that the aortic

vestibule was considerably larger than normal, measuring 5·0 cm. from the free edge of the semilunar cusps to the upper edge of the trabeculated portion of the ventricular cavity, and was excavated by three pockets, measuring from 3·0 to 4·9 cm. in depth, which were extensions downwards of the sinuses of Valsalva.

Only one of these pockets deformed the outer aspect of the heart, that one being the aneurysm of the left sinus of Valsalva ; it forms the bulge visible in Fig. 4 to the left of the pulmonary artery. The other pockets produced no prominence on the outside of the heart.

This observation, that only the aneurysm of the left sinus produced a prominence on the outside of the heart, demonstrates that the aneurysms are dilatations of the sinuses of Valsalva, and not aneurysms of the aorta above the level of the sinuses. For in the normal heart the sinuses of Valsalva belong to the part of the aortic root that is entirely embraced by the heart wall except at one place, just to the left of the pulmonary artery, where a part of the left sinus of Valsalva is supported only by the wall of the aorta.

The cavity of each aneurysm was lined to a large extent by endocardium, which was continuous on the ventricular wall of the cavity (the " anterior " wall when the heart is opened out, as in Fig. 5) with the endocardium of the aortic cusps, and on the aortic (or " posterior ") wall with the intima of the aorta. Much of each cavity was lined by brown adherent blood-clot, and when this was picked off the endocardial lining underneath was seen to be replaced by what appeared to be fibrous tissue. So large a portion of each cavity possessed a smooth endocardial lining that it seems probable that the endo-cardium may once have been continuous over the whole inner wall and that it was destroyed only by organization of blood clots. Removal of the organized blood clot with a dissecting forceps did not in any place disclose a thinning of the wall underneath.

The ventricular wall of each cavity was formed partly by its own cusp, and below the cusp by a uniformly thick partition (about 0·1 cm. thick), which appeared to consist mainly of fibrous tissue. Laterally each cavity narrowed considerably and was separated from its neighbour by a similar partition. The other (non-ventricular) wall of each cavity was formed by the adjacent portion of the myocardium, and the myocardial wall of the cavities did not appear to be eroded or thinned.

The photograph (Fig. 5) shows the interior of the left ventricle, opened by an incision passing through the aorta at the junction of the left with the posterior aortic cusp. The left auricle too is shown opened out and the cusps of the mitral valve can be seen. The arch of the aorta can be identified by its three large branches, and the two coronary orifices can be seen. On the extreme left of the picture part of the cavity of the left auricle can be seen. Next from the left can be seen the cavity of the large left sinus of Valsalva cut across by the incision ; this has just opened the posterior margin, and so a very small part of the cavity is seen on the right of the picture as well (Fig. 5F) just above the attachment of the aortic cusp of the mitral valve. To the right of this is the mouth of the left sinus, the left aortic cusp being pulled upwards

and to the left by the traction on the heart wall required to display the specimen for photography ; the opening of the left coronary artery is clearly seen. To the right again, in the centre of the picture, is seen the mouth of the right sinus (Fig. 5D), with the opening of the right coronary artery just above it. Finally, beside it, is the mouth of the posterior sinus (Fig. 5E) ; both this and the right sinus have been lightly packed with cotton wool for
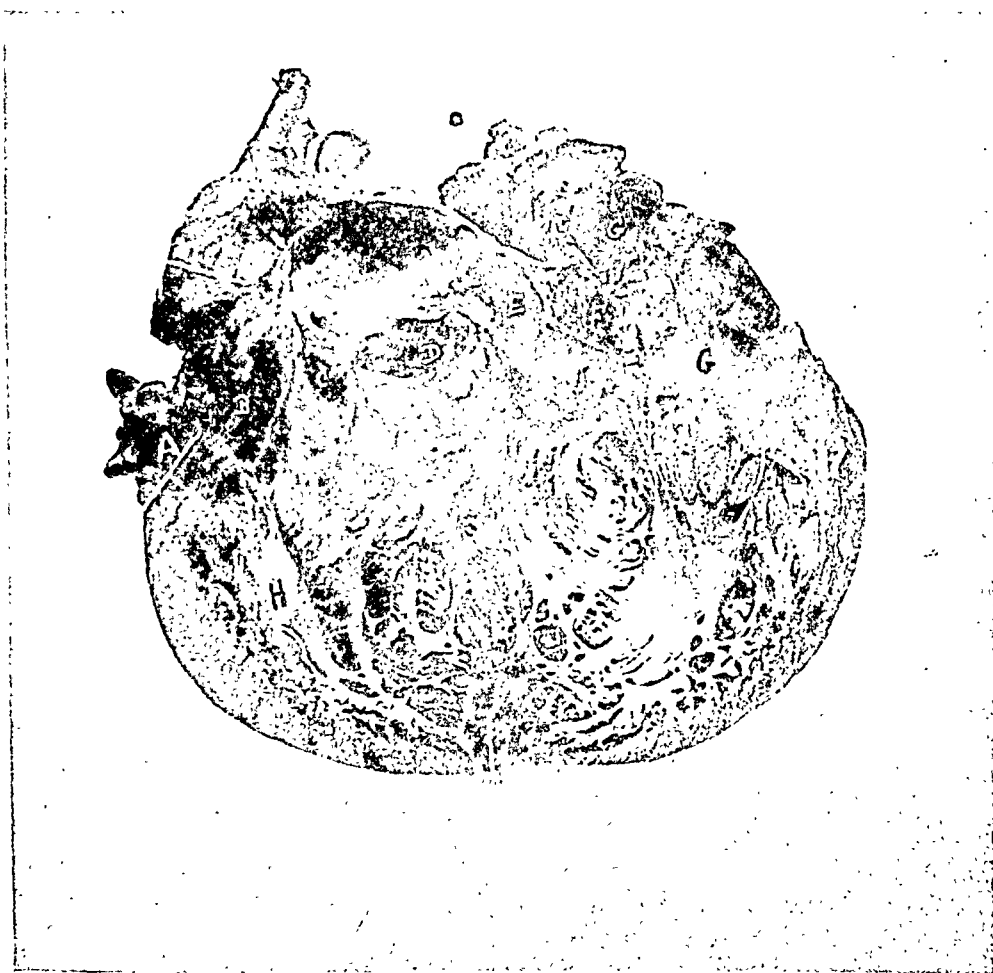

FIG. 5.—Interior of left ventricle.

(A) Part of left auricle. (B) Cavity of left sinus cut across. (C) Opening of left sinus with orifice of left coronary artery just above. (D) Opening of right sinus with orifice of right coronary artery just above. (E) Opening of posterior sinus. (F) Cavity of left sinus cut across (corresponds to (B)). (G) Cavity of left auricle. (H) Anterior papillary muscle. The inferior papillary muscle is seen opposite (H) and below (G).

photographic purposes. To the right again is the mitral valve and the left auricle.

The intima of the aorta is smooth and normal in appearance, but a few yellow streaks are seen about the opening of the right coronary artery. The circumference of the aorta at this level is 7·7 cm.

The three aortic cusps are visible, and behind each cusp is the opening into a grossly dilated sinus of Valsalva, each of these openings measuring about 2·5 cm. in diameter when the tension on the walls of the opened ventricle is relaxed enough to allow them to assume a roughly circular form. The width of the openings is not so great as the length of the aortic cusps, for each opening is separated from its neighbour by a roughly pyramidal buttress over 1·0 cm. thick at its base, to which the aortic cusps are attached. Similar buttresses may be seen serving as the points of attachment of the aortic cusps in many hearts in which the left ventricle is considerably enlarged. They are well shown in the photograph, the buttress between the right sinus and the posterior sinus standing out particularly clearly ; the buttress between the right sinus and the left sinus is less striking ; that between the left sinus and the posterior sinus can be recognized on the right of the photograph by the attachment of the aortic cusp of the mitral valve.

The ends of the aortic cusps are attached to the buttresses springing from the aorta. Thus the aortic cusps lie at a lower level than normal, being in fact over 1·0 cm. lower than the openings of the coronary arteries. The upper level of each buttress lies at about the normal level of the point of attachment of the aortic cusps. In the case of the buttress lying between the posterior and the right sinuses the cusp is continued along the upper aspect of the buttress as a fold of endocardium, which suggests that the low position of the cusps may be the result of traction. The cusps of the pulmonary artery are normal in position, i.e. 1·0 cm. higher than the aortic cusps.

The Posterior Sinus of Valsalva

The posterior (right posterior, B.R.) aortic cusp is of normal thinness, but it alone presents one slight abnormality. The posterior sinus is separated from the anterior by a thick buttress. Similar buttresses exist at the other two points of junction, and in the case of the other two sinuses the aortic cusps are attached to the tip of the buttresses ; but, in the case of the posterior aortic cusp, the end of the cusp that is related to the anterior aortic sinus does not end at its point of attachment to the buttress, but is prolonged along the superior surface of the cusp as a shallow fold of endocardium to the aortic attachment of the buttress. This fold of endocardium is so shallow (under 1 mm. in depth) that it can only just be picked up with the fingers ; its length is 1·4 cm. The cusp proper is 2·8 cm. in length, and the corpus Arantii is situated in the middle of the cusp proper, and not in the middle of the 4·2 cm. long fold of cusp proper plus endocardial fold.

The cavity of the posterior sinus is roughly spherical and 9 c.c. in volume. Its depth, measured from the free margin of the aortic cusp, is from 3·0 to 3·5 cm. It is separated from the right sinus and from the left sinus by thick buttresses. It is related anteriorly to that smooth-walled part of the cavity of the left ventricle known as the aortic vestibule, and posteriorly it bulges into both right and left auricles. It also bulges slightly into the right sinus of Valsalva.

The orifice of the posterior sinus differs from the orifices of the other sinuses in that it is constricted by a thick semilunar fold, less than 1·0 cm. below the aortic cusp. The base of this fold is about 1·0 cm. in length and is attached to the buttress that separates the posterior from the left sinus. The free margin is directed to the right, is about 1·0 cm. distant from the base, and shows a very slight concavity. This fold constricts the orifice of the posterior sinus to a diameter of about 1·0 cm. Below this fold the sinus expands to a cavity of approximately 2·5 cm. in diameter.

The Right Sinus of Valsalva

The right (anterior, B.R.) aortic cusp is of normal thinness and the corpus Arantii can be felt half-way along its free margin, which measures 4·1 cm. in length.

The opening of the right coronary artery may be seen above the right aortic cusp. It is a little less than 1·0 cm. above the plane marking the opening of the sinus, and cannot be described as lying within the sinus. It lies 2·2 cm. from the junction of the right and left aortic cusps and 1·7 cm. from the junction of the right and posterior aortic cusps. It is 2·9 cm. from the orifice of the left coronary artery. Its orifice is of normal size, and a few faint yellow streaks (but not wrinkles) around it suggest a slight degree of atheroma.

The cavity of the right aortic sinus measures 15 c.c. in volume. . Its outline is that of a waistcoat pocket that tapers slightly towards its depth, the greatest depth being 4·0 cm. The cavity has a ventricular aspect related to the smooth-walled aortic vestibule of the left ventricle ; the other aspect is related to both the right auricle and the right ventricle, and it produces very striking prominences on the walls of those chambers. The cavity of the right sinus occupies the whole of the inter-ventricular septum above the level of the line of junction of the aortic vestibule with the main body of the ventricle ; the dilated sinus is in such a position that it would seem to have interfered with the bundle of His, where it straddles the interventricular septum (the pars membranacea), dividing there into right and left branches. Yet there is no thinning of the sinus wall to be detected at this point, alluded to by authors, who have reported cases of aneurysm of the right sinus, as a *locus minoris resistentiœ*.

The ventricular wall of the sinus is formed above by the aortic cusp, which is of approximately normal thinness and depth ; at the attached border of the aortic cusp a sudden transition in thickness is to be noted where the cusp gives place to the thicker sinus wall ; this wall appears to be mostly fibrous, but streaks of reddish strands (presumably muscle fibres) can be seen running up into it from the main body of the ventricular wall below.

The Left Sinus of Valsalva

The left (left posterior, B.R.) aortic cusp is of normal thinness, and the corpus Arantii can be felt half-way along its free margin. As the ventricle

was open by a cut that divided the aorta close to the cusp, this is more curled on itself than the other two. When straightened by gentle traction its free margin measured 3·7 cm.

The dilated left sinus of Valsalva is by far the most striking of the three " aneurysms," for it is the largest and is also the only one that is directly related to the external surface of the heart ; it forms the prominence so clearly seen in Fig. 5 to the left of the pulmonary artery.

It would have been almost impossible to have opened the left ventricle without opening up one of the sinuses in some place, and fortunately the incision does not pass across the middle of the cavity, but opens it at its extreme posterior border near the aortic cusp of the mitral valve.

The volume of the left sinus is hard to measure owing to the incision made, but it holds over 50 c.c. and probably between 60 and 70 c.c. The greatest depth of the cavity is 4·9 cm. and its greatest breadth 6·9 cm. It extends downwards from the free margin of the left aortic cusp to about the line of junction between the aortic vestibule and the main body of the ventricle. Internally it is related to the cavity of the left ventricle. Externally it bulges into the pericardial sac to the left of the pulmonary artery. It is not related to any of the other chambers of the heart, but it extends the whole way across the upper part of the left ventricle from the inter-ventricular septum in front and to the right to the attachment of the aortic cusp of the mitral valve behind and to the left.

The orifice of the left coronary artery lies a little above the point of junction of right and left aortic cusps, being thus outside the sinus.

I have presented the clinical and anatomical record of this unusual case as fully and accurately as I can, and leave it for those who are competent to discuss it. The term " congenital aneurysm " was used in the title of this paper, because I cannot think of any morbid process capable of producing the condition described after the stage of development is past.

DISCUSSION

In most text-books aneurysm of the sinuses of Valsalva receives only the briefest mention, and the usual causes described are syphilis and ulcerative endocarditis. I have not attempted to survey the subject of aneurysms of the aorta involving one or more of the sinuses of Valsalva, but only those communications that record an abnormal dilatation of all three sinuses.

Instances of presumed congenital aneurysm of one sinus have been recorded, the sinus affected being in nearly every case the right (or anterior) sinus. These aneurysms are discussed by Maude Abbott (1927 and 1932). Henke and Lubarsch (1924) also devote several pages to the subject.

I have been able to find only three records of cases with aneurysms or pathological dilatations of all three sinuses, those of Carpentieri (Naples), of Barnscheidt (Bonn), and of Habán (Budapest).

Carpentieri's case (1912).—The patient died after an illness of four days. He was 45 years old and a deaf-mute, so that it was difficult to take a history of the illness. He was too sick for thorough examination, but œdema of both lower limbs was recorded. The apex beat was 3·0 cm. outside the mid-clavicular line in the sixth space. There was a presystolic-systolic murmur audible at the apex and a systolic murmur at the aortic area. There was no record of the heart rhythm.

The heart was enlarged, measuring 12·0 cm. at its base by 12·7 cm. in its greatest length. The left ventricle, which was responsible for most of the enlargement, was enormously dilated ; its walls were 2·3 cm. thick, and the mitral orifice was dilated and admitted three fingers easily, but was not incompetent, in Carpentieri's opinion, as the dilatation was compensated for by the length of the cusps.

The aortic cusps were thickened and shortened by " atheromatous scars," but the aortic orifice was nevertheless normal. The aorta itself showed " atheromatous scars."

The three sinuses of Valsalva were represented by three large cavities, but their position is obviously different from that in our specimen, for they are described as presenting swellings about the size of a nut on the exterior of the aorta. Another important difference is that the lower limit of each cavity was formed by the attachment of the cusp, whereas in our specimen the cusps are attached to the anterior wall of the cavity, which extends downwards about 4 cm. below the level of their free margin. Neither the relations nor the size of the three sinuses were carefully described, but the left was mentioned as being the largest and as excavating a small tract of the upper wall of the left ventricle. The walls of the sinuses, especially of the left, were very thin (*sottilissime*).

No abnormal communication existed between the chambers of the heart, or between the aorta and pulmonary artery.

There was, in the author's opinion, no evidence of syphilis ; but the patient died early in 1911, and apparently no test was done on his serum ; the " atheromatous scars " described on the aorta and the aortic cusps should be noted.

Barnscheidt's case (1920).—This has not been published, but is mentioned by Henke and Lubarsch. The specimen was described by Barnscheidt in 1920. I wish to express my gratitude to the authorities of the Bonn University Library for· their great courtesy in lending me the thesis presented by Dr. Barnscheidt for his doctor's degree.

The heart was a museum specimen, the clinical history of which was not

known. It was described as " relatively small." The wall of the left ventricle had a greatest thickness of 1·9 cm. and an average thickness of 1·4 cm. The aorta was healthy and the aortic orifice had a circumference of 5·3 cm. The myocardium and endocardium appeared healthy.

The aortic cusps were unusually thin and shiny and greatly altered in configuration through the part which they took in forming the aneurysms. Each sinus showed a marked dilatation (*eine erhebliche Ausbuchtung*), the depth of the right and posterior sinuses being about 1 cm., while that of the left sinus was less. In all three sinuses the direction of the dilatation was sideways and horizontal, but also downwards in the direction of the left ventricle. The surfaces of contact of the cusps were thus increased in breadth to about 4 mm. On the inferior margin of these surfaces a swelling about 2 mm. thick had formed, on which slight verrucosities were to be found. These changes were best marked on the posterior cusp.

The dilatations were not all of the same volume ; the posterior sinus was the largest, the right was slightly smaller, while the left was considerably smaller with a depth of only about 0·5 cm. measured horizontally. No perforations were present.

Barnscheidt gave it as his opinion that the aortic valve cannot have been incompetent ; the possibility of some degree of aortic stenosis cannot, he thinks, be so readily denied, as the aneurysmal sacs hanging down into the left ventricle may well have given rise to some narrowing of the aortic orifice. The endocardial changes on the inferior surfaces of the aortic cusps must have been secondary.

Barnscheidt gave no measurements apart from those we have quoted, but the thesis contains a photograph of the specimen that suggests that the " aneurysms " were very small. The heart was a formalin-specimen in the museum and the difficulties of examining and photographing such an old hardened preparation must have been very great.

Habán's case (1937).—A man, aged 46, was admitted to St. Stephan Hospital in Budapest three days after duodenal perforation. He died some hours after operation. Nothing was reported about his previous history.

The heart showed syphilitic changes confined to the sinuses of Valsalva and the aortic cusps, but Habán holds (with reason, we think, judging by his description) that the syphilitic process was not the cause of the aneurysms, and that an abnormal dilatation of all three sinuses must have already been present. The degree of dilatation was slight, the right sinus being the largest ; it was described as being large enough to admit completely the terminal phalanx of the thumb. The posterior sinus was the next largest, and the left sinus the smallest, being described as *markedly larger than normal*.

SUMMARY

1. A case is described in which aneurysms, or more correctly gross dilatations, of all three sinuses of Valsalva were present.

2. The left ventricle was considerably hypertrophied, but apart from this and the aneurysms the heart was healthy. There was no evidence of syphilis or endocarditis, recent or old-standing. There were no perforations or abnormal communications between the chambers of the heart.

3. The aneurysms were deep (nearly 5·0 cm.) pocket-like extensions of the sinuses of Valsalva in a downward direction. They excavated the smooth-walled part of the ventricle described as the aortic vestibule, but not the thick trabeculated portion of the wall. Their symmetry, their endocardial lining, and the absence of syphilitic or ulcerative changes were strongly suggestive of a congenital abnormality.

4. The aneurysm of the left sinus measured over 60 c.c. in volume. It formed a prominence on the surface of the heart to the left of the pulmonary artery.

5. The aneurysm of the right sinus measured 15 c.c. in volume. It bulged into both the right auricle and the right ventricle. The presence of this aneurysm in the interventricular septum is believed to have produced the heart-block from which the patient died.

6. The aneurysm of the posterior sinus measured 9 c.c. in volume. It bulged into both the right and left auricles.

7. The patient was free from symptoms of heart disease till a few months before his death. He died from acute cardiac failure and complete heart block, and during his last illness several interesting disturbances of rhythm occurred.

8. Records of three other cases of aneurysm of all three sinuses of Valsalva have been found and discussed. In all the degree of dilatation was considerably less than in the case here recorded, and the direction of the excavation appears to have been different.

F

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A SINGLE CORONARY ARTERY

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Many different anomalies of the coronary vessels have been observed. The minor varieties are quite common, but the more gross forms are relatively rare. An example of one of these gross forms is given in this paper.

The variations may be divided into a number of groups : (1) in origin, (2) in number, and (3) in distribution and size.

Anomalies in origin are due to the vessel starting abnormally : (a) from the common arterial trunk, and this is often found where there are other associated disturbances of development ; (b) from the pulmonary artery, when changes develop secondarily both in the artery and in the myocardium, changes that depend directly on this aberrant origin of the vessel ; and (c) from the aorta, at a variable distance above the level of the cusps.

Anomalies in the number of vessels are rather more common and may be unusual by a reduction or by an increase in the number ; thus on the one hand there may be only one artery arising from the aorta, or on the other hand there may be three, four, or more vessels. As far as their supply to the myocardium is concerned they merely take the place of the normally occurring vessels in most instances. Thus a single artery is usually much larger and gives a supply to the whole of the heart, whereas an increased number of vessels are individually smaller and correspond in their distribution to one or more of the branches of the normal arteries.

Anomalies in distribution and size depend to a considerable extent on, and run *pari passu* with, anomalies in the number of main trunks.

CASE REPORT

A man, aged 45 years, died from a lobar pneumonia after six days' illness. There was consolidation of the lung, affecting the basal and middle portion of the left lung and the basal lobe of the right lung. There were toxic changes in the liver, spleen, and kidneys. The pericardium contained about 2 oz. of straw-coloured fluid. The heart weighed 16 oz. and showed a thickened left ventricle, which was somewhat dilated also. The valves were normal. There were some atheromatous patches on the proximal part of the aorta.

The coronary vessels presented an unusual distribution in that there was only one main orifice, which arose from the right sinus (Fig. 1). This opening was large, being 9 mm. in diameter. There was no suggestion of an orifice in the left sinus. In the depths of the orifice there could be seen three openings, of which one was large and the other two, lying in front of this, were small (Fig. 2). On the exterior three vessels arose from the main region of the
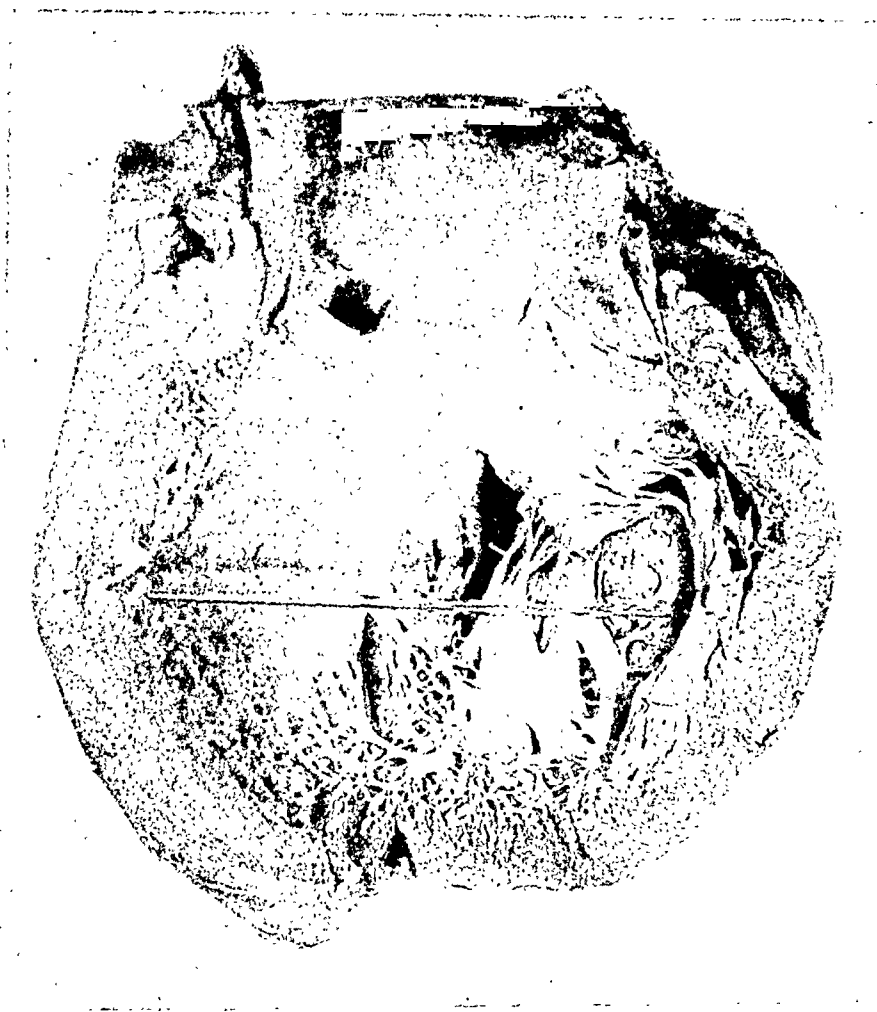

FIG. 1.—Photograph of the heart, opened to show the left ventricle and aorta. The large orifice of the right coronary artery is visible in the right sinus, but there is no corresponding opening in the left sinus.

aorta, at a position corresponding to that usually occupied by the right coronary artery.

The *first* and largest trunk corresponded to a right coronary artery and ran, in the usual manner, in the coronary sulcus, but differed from the usual course in that it passed round the heart to terminate on the anterior aspect, near the anterior longitudinal sulcus (Fig. 3). In its proximal part it was 6 mm. in diameter and much more tortuous than usual, but its walls were of normal thickness. At the right border of the heart it gave a large marginal branch

A SINGLE CORONARY ARTERY

which passed down the margo acutus to supply this portion of the right ventricular wall. On the posterior aspect of the heart there was another large branch, passing distally and supplying the posterior aspect of the right ventricle. In the region of the posterior inter-ventricular sulcus a large branch
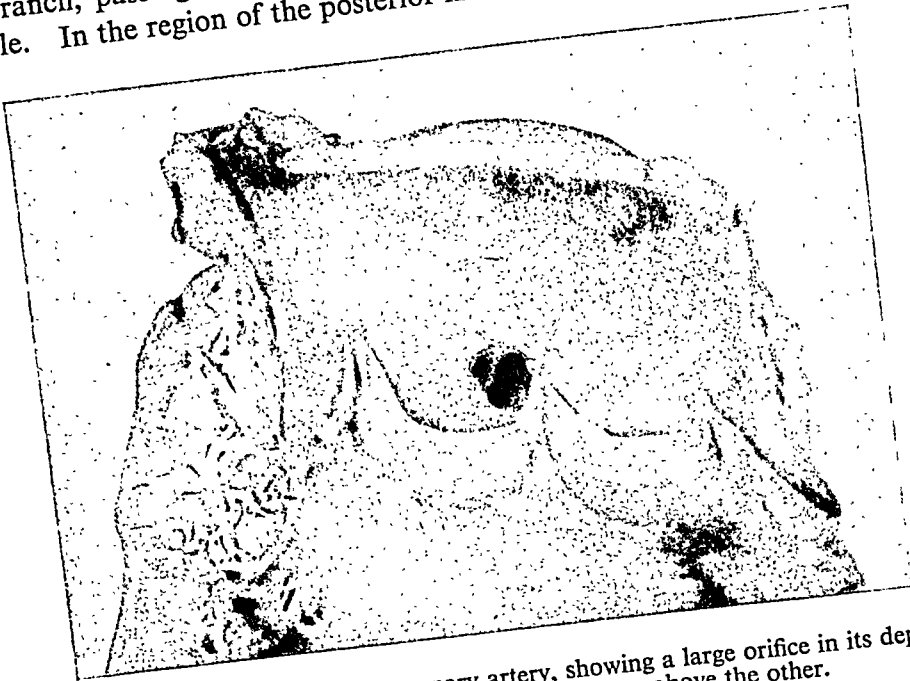
FIG. 2.—A closer view of the coronary artery, showing a large orifice in its depths and two smaller openings to its right, one above the other.

FIG. 3.—Diagram to show the distribution of the vessels. Arising from a common origin on the right side of the aorta are three trunks: a large vessel, corresponding to the right coronary artery, passing right round the heart in the coronary sulcus; a small intermediate branch running down on the front of the right ventricle; and a large vessel running across in front of the aorta and pulmonary artery, and turning down to occupy the anterior inter-ventricular sulcus. There is an anastomosis between this and the termination of the first vessel mentioned.
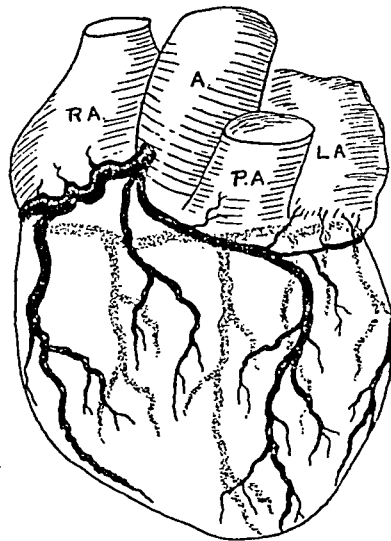
(corresponding to the posterior descending branch) passed down the sulcus, giving branches to both ventricles and terminating in the region of the apex. In that part of the course of the main artery just described there were smaller branches distributed to the adjacent arterial and ventricular walls.

After giving off the posterior descending branch, the main artery continued

in the coronary sulcus, and gave further branches to the ventricles (*rami collaterales*), to the atrium, and a left marginal branch which ran down the margo obtusus. It then passed round on to the anterior aspect of the heart and anastomosed with an anterior artery (to be described). From all the vessels described small branches passed into the myocardium, and some larger arteries passed into the region of the septum from the main artery and the posterior descending branch.

The *second* trunk, arising from the common opening in the sinus, passed down over the front of the right ventricular wall and divided into numerous small branches about half way down this wall.

The *third* trunk, arising in the common orifice on the left side of the two just mentioned, ran across the upper part of the right ventricle in front of the aorta and pulmonary artery. On reaching the anterior longitudinal sulcus it passed downwards in this to the apex. It gave numerous branches—to the pulmonary artery (infundibular branch), atrial rami, and deep muscular branches, the largest being in the region of the septum. At the apex of the heart this anterior descending branch appeared to anastomose with the terminal rami of the posterior descending branch. At the point where the vessels entered the anterior longitudinal sulcus, there was a small anastomosis with the terminal part of the large right coronary vessels.

DISCUSSION

Several classical cases of " absence " of the left coronary artery have been recorded, notably those of Bockdalek (1867), Gallavardin and Ravault (1925), Smith and Graber (1926), Grätzer (1926), Kintner (1931), Born (1933), and Sanes (1937).

The origin from the aorta is very variable and usually consists of one orifice and one main trunk that divides into two (Gallavardin and Ravault) or three (Bockdalek) branches. On the other hand two (Kintner) or three (Grätzer) separate openings have been found in the same sinus.

The course of the vessels is also subject to considerable variation. In most of the cases (Bockdalek, Gallavardin, and Ravault, Kintner, Born, and Sanes) one vessel passes from the origin deeply into the interventricular septum and after traversing this appears at some point on the anterior longitudinal sulcus where it continues as an anterior descending branch.

In the case described by Smith and Graber, as in that recorded here, the anterior descending branch arises from a vessel running in front of the conus ; the distribution of the vessels, however, is different.

From consideration of these various cases the explanation of the anomalies is simple. Thus various anastomotic vessels become enlarged and, as in other parts of the body, become sufficiently important to replace the ordinary vessels. This is easily seen by comparison of the two diagrams shown in Fig. 4.

In the present case there is a great enlargement of the right coronary artery, which replaces the circumflex branch of the left coronary artery. In addition

the anastomotic vessels between the right and left coronary vessels in front of the conus (Konus-anastomose) have become the significant supply of the area usually supplied by the anterior descending branch of the left coronary.

The reason for such aberrant development cannot be known accurately and the various hypotheses—in the absence of definite evidence of vascular disturbance in fœtal life—do not warrant discussion. The blood supply to the myocardium in these cases is, in the absence of acquired disease of the
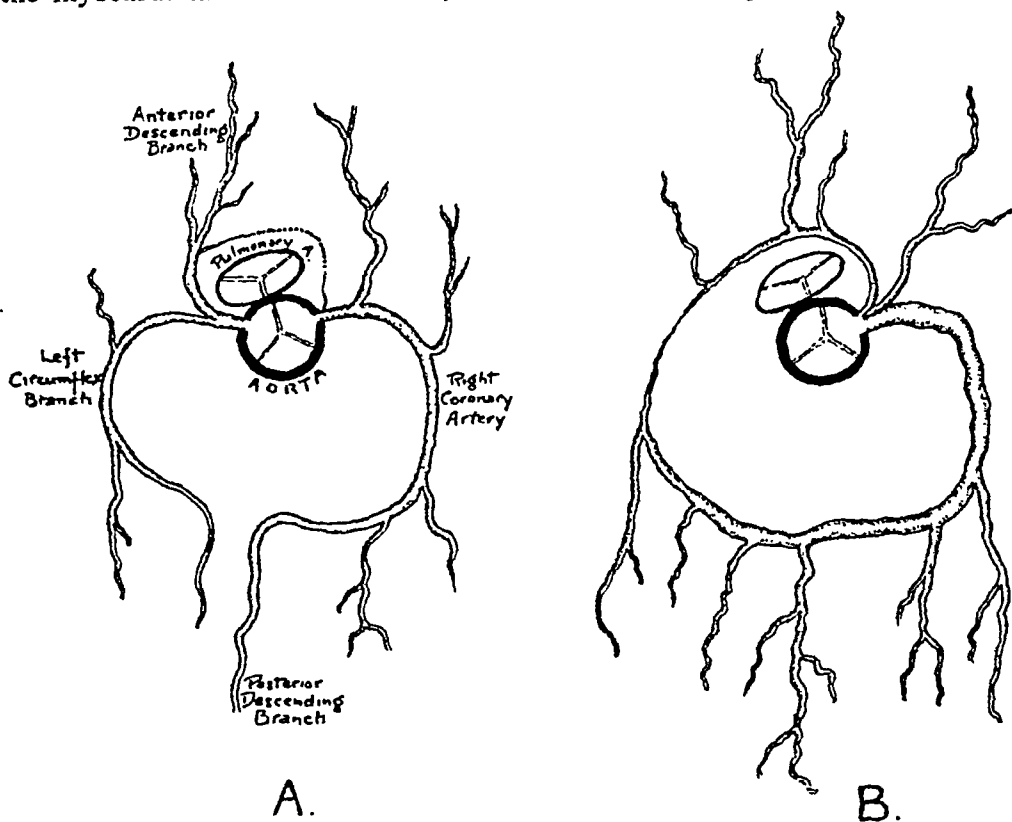
Fig. 4.—Diagram to show the relationship of the vascular distribution in a normal case (A) and in this case (B).

(A) The two vessels, right and left coronary arteries, are shown with their principle branches. The dotted line indicates a small anastomosis in front of the pulmonary artery—the conus anastomosis.

(B) The large vessel that arises from the right sinus and immediately divides into three is shown. The main vessel corresponds to the right coronary artery and most of the left circumflex branch. The intermediate vessel corresponds to an anterior branch of the right coronary artery. The left vessel occupies the position of the conus anastomosis and corresponds in distribution to the anterior descending branch and a small part of the left circumflex branch.

vessels, sufficient for the supply of the myocardium, and the actual route taken by the blood is of little consequence.

The blood supply to the myocardium is thus merely a variant of the normal arrangement, " absent " vessels being replaced by branches of other arteries that follow much the same course as the " absent " vessels would.

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SUMMARY

A case of a " single " right coronary artery has been described and also its distribution to the myocardium. The large artery immediately divided into three branches. The main vessel took the usual place of the right coronary artery and of most of the circumflex branch of the left coronary artery. The intermediate vessel took the place of an anterior branch of the right coronary artery. The third, passing along the usual site of the small conus anastomosis, took the place of the anterior descending branch of the left coronary artery.

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THE ELECTROCARDIOGRAM IN PELLAGRA

BY

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Deficiency in thiamin, a factor of the vitamin B complex, may cause severe circulatory insufficiency. It is, therefore, of interest to study the circulation in another type of B-avitaminosis—pellagra.

The circulatory disturbances encountered in pellagra are of no great clinical significance. Frequently low arterial pressure and tachycardia are present. Œdema, if there is any, can scarcely be attributed to circulatory insufficiency, even if exclusively present at the lower extremities. As shown by the example of beri-beri and the famine œdema, this accumulation of fluid is especially connected with changes of the tissue itself and the composition of the plasma.

For these reasons it is particularly the electrocardiogram that is dealt with in this paper. As far as we know only Porter (1934) and Feil (1936) have studied this question. The former found nothing more than sinus tachycardia ; the latter, who investigated 38 pellagra patients, found in 14 of them electrocardiographic changes that could not be attributed to other circulatory disturbances. There was sinus tachycardia, low voltage of the ventricular complex, a high T, a Pardee-type of T, an abnormals hape of the S–T portion, as well as a negative T wave. In the chest lead also some abnormalities were found, e.g. low voltage, M-shape of the ventricular complex, a monophasic S–T, or an upright T. The changes in the electrocardiogram gradually disappeared, in part, when the pellagra itself was cured, thus revealing their relationship with the disease.

PRESENT INVESTIGATION

We have 45 electrocardiographic records of 23 pellagra patients (15 men and 8 women) ; 21 suffered from the chronic type of the disease and 2 from a first attack of the acute type (Cases 21 and 22). Eight of the men and one woman were over 50 years of age. This is of some significance since, with advancing age, the possibility of cardiographic changes due to coronary sclerosis increases, even without clinical symptoms. We therefore separated our material into two groups, below and above this age. Patients who had circulatory symptoms clinically were excluded from these investigations. The blood pressure of the patients varied from 85/55 to 190/95 mm. In one only

was there a high arterial pressure ; but his cardiogram showed nothing abnormal. In all the others the pressure was below 150 mm. Some of the individual data may be seen in Table II. No drugs likely to influence the shape of the cardiogram (e.g. digitalis, quinidine, etc.) were given. In all 23 the cardiogram was taken immediately after the patient's admission ; in 11 of them additional records were taken once or more during their stay in hospital.

The records were taken with an amplifier electrocardiograph in the three classical leads, and in 18 cases with the chest lead too (apex of the heart—left leg).* The electrodes were connected in such a way that in normal cases T was negative. The standard gauge of amplitude was 10 mm.=1mV.

RESULTS

The results of these investigations are shown in the following tables and figures. Among the abnormalities observed, the most frequent was sinus tachycardia, which occurred in about one third. In one patient (Case 18) it was not certain, on account of his high temperature, whether there was an actual connection between this cardiac phenomenon and the pellagra. Similar findings were also obtained in some older persons, where they were particularly striking in view of the senile bradycardia.

Table I shows that in nearly half of the cases the electrocardiogram was normal, and also that the abnormalities observed were of various types. Alteration of the S–T interval and of the T wave were present in all the pathological records (13 out of 23). Moreover, there was frequently deformation of the ventricular complex (low voltage or notching) in a total of six cases. Pathological manifestations of this kind in lead IV were presented by practically half the patients (see Table I).

TABLE I

ELECTROCARDIOGRAPHIC ABNORMALITIES IN PELLAGRA

Electrocardiographic Findings	Number of Cases	Number over 50 Years of Age	Percentage with this Abnormality
Normal records	10	2	—
Abnormal records	13	7	57
Sinus tachycardia (90 or over)	9	7	39
Auricular fibrillation (1 case) or Ventricular extrasystoles (3 cases)	4	1	17
Low voltage of QRS (below 5 mm.) ..	2	2	9
Notching of the QRS (4) or Large Q_3 (1)..	5	3	21
S–T interval above or below zero level ..	3	1	13
Negative T_1 (1) or negative T_2 and T_3 (1)	2	1	8
Abnormalities of lead IV (18 cases only) ..	11	4	61
Low voltage	3	1	16
Notching of R (3) or M form of QRS (2)	5	3	27
Upright T (4) or Absent T (3)	7	2	39

* It will be seen that the lead IV records were taken before the publication of the recommendations of the Cardiac Society and the American Heart Association and do not conform to these recommendations.

The findings in these records show no features characteristic of pellagra. Two clinical arguments, however, favour the assumption that the disturbances have some causal relationship with pellagra.

The first argument is the high incidence (57 per cent.) of a pathological electrocardiogram in pellagrins with an otherwise normal circulation. This holds true even remembering that in older persons such findings may result from coronary sclerosis without clinical symptoms and that half our patients with a pathological electrocardiogram were over 50 years of age. On the other hand, there was a very abnormal electrocardiogram in one female pellagrin of 23, who subsequently succumbed to the disease.

The second and decisive argument concerns the parallelism between the course of the disease and the development of the electrocardiogram, in cases either with improvement or even cure and in those with deterioration or death. Decisive proof, however, is furnished by the fact that the pathological electrocardiogram returned to normal, parallel to the proceeding improvement of the process ; while such an occurrence could scarcely be expected if the changes were due to coronary sclerosis (apart from the occurrence of acute infarction). Other irreversible heart affections that might have induced the electrocardiographic symptoms could be ruled out by the clinical findings.

TABLE II

CASES OF PELLAGRA WITH ABNORMAL ELECTROCARDIOGRAMS *

Case Number	Age	Sex	Blood Pressure	Rate	Abnormalities
1	50	M	95/55	70	Extrasystoles, S–T above zero level (II, III).
4	50	M	110/70	78	Flat T_1, Upright T_4.
6	46	M	110/55	80	Flat T_1, Low voltage lead IV
9	70	M	135/70	115	$S-T_2$ below zero level
10	60	M	110/65	92	Low voltage, Absent T_2
11	54	M	145/80	79	Notching of QRS_3, M complex of QRS_4, Absent T_4
12	66	M	130/80	72	Notching of QRS_2 and $_3$, Flat T_1, Negative T_2 and T_3
13	55	M	90/70	88	Flat T_1, M complex of QRS_4
14	58	M	120/70	85	Low voltage, Notching of QRS_2, M complex of QRS_3
17	36	F	95/60	120	Flat T_1
18	23	F	95/55	120	Absence of T_1, T_2, and T_4, Low voltage lead IV
22	46	F	120/80	85	Large Q_3, S–T depressed (I, II), Negative T_1, Flat T_2
23	80	F	110/80	110	Aur. fib., Notching of QRS_2 and $_3$, Absent T_4

* From several records of the same patient, we have chosen, in this Table, the most characteristic one.

Table II is supplementary to Table I and gives a brief description of the clinical data and pathological records observed in the 13 pellagra patients, who had such abnormal records. There were a total of 11 cases in which we had the opportunity of following up the development of the electrocardiogram.

Details of these 11 cases follow and they could be divided into three groups—those with no electrocardiographic change after recovery (3 cases), those with electrocardiographic improvement after treatment (3 cases), and those with the electrocardiogram becoming worse as the disease progressed (5 cases).

Group I.—Cases with No Electrocardiographic Change after Recovery

In three cases no change of the cardiogram was observed after recovery following nicotinic acid treatment.

The first (Case 21) had acute pellagra (first attack) and the cardiogram was normal from the beginning.

In the second (Case 7) conditions were similar. A woman, aged 46, suffered from a mild type of pellagra, the duration of which could not be determined from the history. At the climax of the disease the cardiogram showed no pathological features, and during recovery there were no changes except a moderate increase of T, which had been normal from the beginning in all three leads.

The third was a woman of 80 (Case 23). Although the pellagra symptoms rapidly improved (diarrhœa, psychic manifestations, and dermatitis) the pathological cardiogram—possibly arteriosclerotic in nature—persisted unchanged throughout the 18 days' of observation.

Group II.—Cases with Electrocardiographic Improvement after Treatment

In the second group (three patients, all treated with nicotinic acid) decrease or disappearance of the pathological character of the cardiogram was observed, parallel to the clinical improvement of the pellagra.

It must be admitted that the first two did not show such peculiarities of the cardiogram, even at the climax of the process, that the record could be called pathological (and they are, therefore, not recorded in Table II). The records taken during convalescence, however, differed greatly from the earlier ones, so that it appears that these had been pathological.

Case 15.—A man, aged 65, was under observation for two months in 1939. Since 1934 there had occasionally been diarrhœa. He showed moderate glossitis and the typical pellagra dermatitis of the backs of both hands, which was suggestive of a long-standing process. Nicotinic acid rapidly caused the disappearance of these symptoms, the old pellagra skin coming off in pieces.

The first cardiogram showed no pathological change. Another, taken no more than 5 days later, showed slowing of the rate from 100 to 83 and an increase of the ventricular complex in all leads, as well as a more distinctly formed S_4, this having been but rudimentary in the first record.

Case 5.—A boy, aged 5, had been under clinical treatment for alimentary anæmia accompanied by cutaneous hæmorrhages in 1938. Then he was again in hospital for pellagra for three months to March 1939. There was frequent diarrhœa, glossitis, hyperkeratosis of the arms, pigmentation of the face, and a hypochromic anæmia. With an adequate diet and vitamins A, D, and C, as well as nicotinic acid, iron, and liver extract, the symptoms subsided.

The first cardiogram could not be called pathological. It presented a large T_1, a large T_2 and a slightly negative T_3 with a pulse rate of 95. In the record taken towards the end of the treatment T was more distinctly separated from S–T in leads I and II. Q_3, which had been present previously, had disappeared and T_3 had become positive.

Case 22.—A woman, aged 46, who had been under clinical treatment from February to May, presented pellagra dermatitis of the backs of both feet of five months duration. There were psychic changes in addition, but no particular digestive troubles. Nicotinic acid treatment improved the psychic condition within a few days and later the skin symptoms.
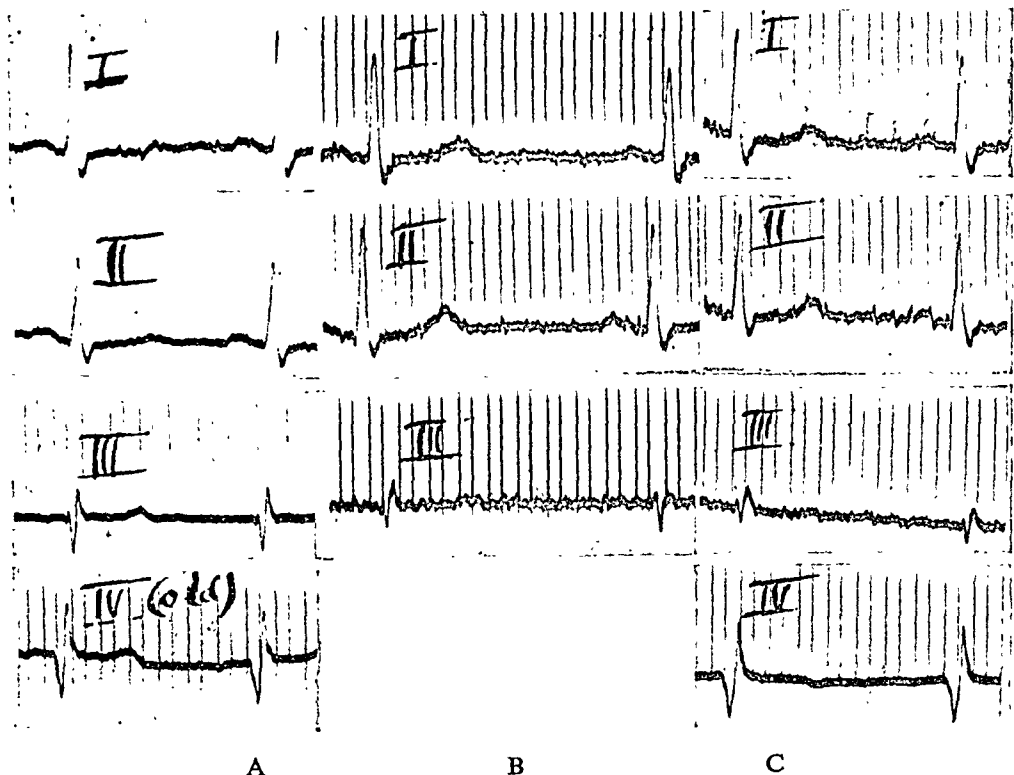
FIG. 1.—Cardiogram improving with recovery from pellagra (Case 22) ; (A) before treatment was started, showing flat T waves in leads I and II and changes in the isoelectric level of S–T ; (B) and (C) after treatment for 18 and 24 days, showing improvement in the T waves in leads I and II (see text).

The first cardiogram (Fig. 1) was pathological. S–T_1 was below the isoelectric level, and there was only a suggestion of T_1 ; S–T_2 and T_2 had melted into a straight line slightly upwards, S–T_4 was above the zero level, and T_4 was positive. In the record taken 18 days later S–T_1 and S–T_2 were on the zero level. T_1 and T_2 were positive, well developed, and distinctly separated from the S–T_1 interval. S–T_4 was now on the isoelectric level and T_4 was absent.

Group III.—*Cases with the Electrocardiogram becoming Worse as the Disease Progressed*

The third group included 5 patients all of whom belonged to the period before nicotinic acid treatment was introduced into the therapy of pellagra. In all of them the cardiogram became more pathological in the course of the process.

This occurred in two patients during their stay in hospital. One responded insufficiently to the treatment (yeast and liver extract) and another did not respond at all. In the three others the pathological development of the cardiogram appeared during relapses at home, after the first attack had readily responded to the treatment. The relapses had been caused by a return to their usual diet. As in the second group, these patients could be separated into those in whom the curves were at first normal or practically normal (although the pellagra process was already present) and the development of pathological signs occurred later, and those in whom the cardiogram was abnormal from the beginning and became more so during the course of the disease. Most of the cases of this group were of the type in which, at the beginning, the cardiogram showed insignificant changes that by no means ranked as abnormal, but took on a pathological character during the development of the disease.

Case 13.—A man, aged 55, had been admitted to the hospital in spring 1937 for chronic pellagra with diarrhœa, dermatitis, and psychic disturbances. After two months' treatment with yeast and liver extract he was discharged without symptoms. In November he was re-admitted with a relapse, which had begun 20 days earlier with diarrhœa. The same treatment that had been given during his first admission was not so satisfactory and the intestinal troubles persisted.

We have at our disposal four records of this patient, three taken during his first stay in hospital and one in the relapse. The first showed nothing pathological. The two following (taken at intervals of one month) were characterized by a diminishing voltage of T_1, although the clinical improvement progressed. Eight months later (during the relapse) this decrease of voltage had reached such a degree that T_1 was now scarcely to be seen. $R-S_3$ showed notching in this last record. In lead IV S–T and T had assumed a pathological shape, but the corresponding lead of the previous records was not at our disposal. The excursion of the ventricular complex, however, did not change.

Case 6.—A man, aged 50, was admitted to the hospital on account of pellagra in February 1938. There were typical changes of the skin on the face, neck, and hands. He had been suffering from diarrhœa for six weeks. Two months' treatment with yeast and liver extract caused the disappearance of his symptoms. Four months later (August), he was re-admitted with a relapse. No notes of his further course are available.

The cardiogram taken at the climax of the disease was not pathological. That, however, taken during the relapse (August) showed marked decrease of the voltage of the ventricular complex in all leads. There was only a suggestion of T_1, and T_2 had become smaller. $S-T_3$ and T_3 had melted into a slightly inclining convex line, and so had $S-T_4$ and T_4, except that in the latter the line declined slightly. The cardiogram had, therefore, become pathological.

Case 14.—A man, aged 58, was under clinical treatment for pellagra from May to August 1937. The skin of his hands had been affected two years earlier. For six months he had been suffering from diarrhœa. After ten weeks' treatment with yeast and liver extract the pellagra dermatitis disappeared, while the diarrhœa improved but had not subsided altogether when he was discharged.

The first record showed notching at $R-S_3$ at its base. The $S-T_3$ interval and T_3 had melted into a slightly convex curve. In the record taken one month later the ventricular complex as well as T had decreased in voltage in all three classical leads. At the top of R_2 notching has appeared and in lead III the ventricular complex has assumed an M shape (Fig. 2).

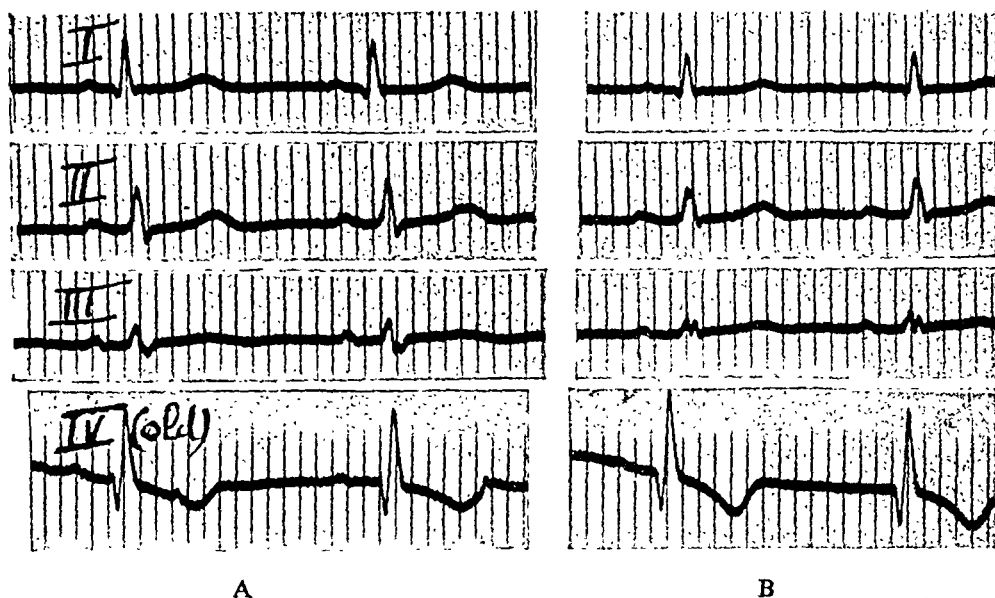A   B

FIG. 2.—Cardiogram showing deterioration as the pellagra became worse (Case 14).
(A) July 7.   Flat T in lead III : (B) August 4.   Diminishing voltage and T waves (see text).

Case 17.—A woman, aged 36, was under treatment from November 1936 to January 1937.   Her pellagra had set in three months before her first admission.   In the early stages there had been a painful glossitis and a dermatitis of the hands, and later pronounced psychic disturbances.   The abnormal excitability of this patient (it was during the pre-nicotinic era) rendered every attempt at suitable treatment impossible.   Three times she left hospital during an attack of depressive agitation and remained at home for several days.   In view of these conditions, the disease proceeded, and in January 1937 she died.

The first cardiogram was normal.   In a later one the voltage of the ventricular complex had decreased and T_1 was scarcely recognizable. T_2 and T_3 had also become smaller and showed a growing tendency to fuse with the preceding S–T interval (Fig. 3).

A   B
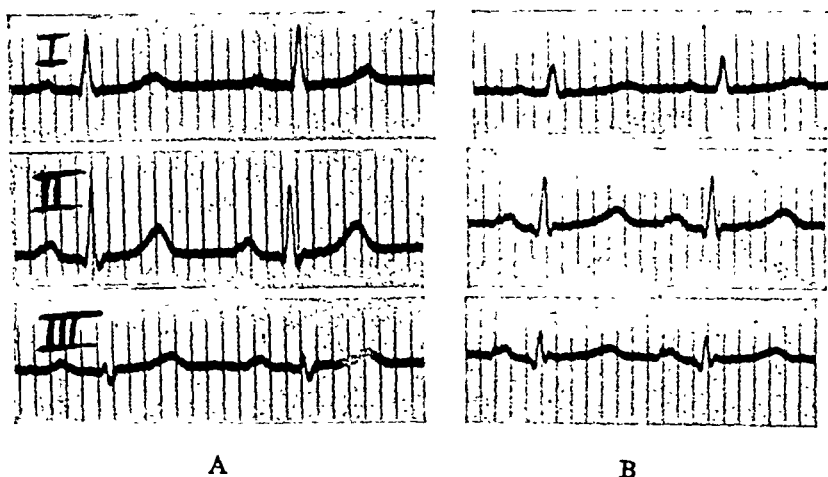
FIG. 3.—Cardiogram deteriorating in a fatal case of pellagra (Case 17).
(A) November 1936.   Normal ; (B) January 1937.   Showing voltage becoming lower and T waves flatter.

Case 18.—A woman, aged 23, had been under treatment for severe pellagra from May until her death in August 1937. The disease had started with diarrhœa in March and it was a febrile pellagra of the severest type, with dermatitis of the hands and feet, psychic disturbances, and anæmia. Large doses of yeast and liver extract improved the anæmia, but she succumbed to the disease.

The first cardiogram was of normal voltage, but T_2 was practically absent and in lead III the ventricular complex was M shaped and T_3 was negative. In the subsequent records, taken at intervals of 3–5 weeks, the voltage was gradually reduced, and in the last record, T_1, T_3, and Q_4 had disappeared. This group of cardiograms shows instructively the progressive increase of the pathological character (Fig. 4).
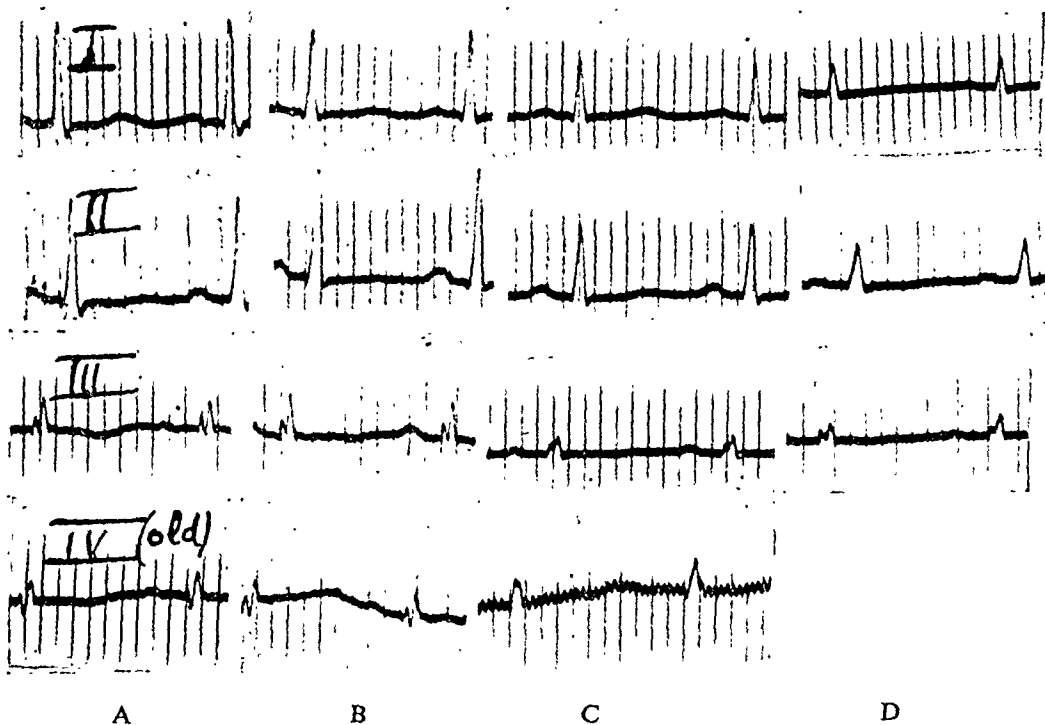
FIG. 4.—Cardiogram deteriorating in a fatal case of pellagra (Case 18).
(A) May 11. Flat T in lead II ; (B), (C), and (D) June 23, July 19 and August 4. Showing voltage becoming lower and T waves flatter.

The P–R interval was on the whole normal, between 0·12 and 0·20 seconds. In three instances it was below 0·12 seconds. One child of five, where P–R was 0·11 sec. cannot be called abnormal (Case 22). The two other findings of this type, however where P–R was 0·10 sec. (Case 10) and 0·11 sec. (Case 13), were certainly pathological.

The duration of the electric systole as measured by the Q–T interval was not characteristically changed. This was plotted out in a diagram, comparing it with the pulse rate, but with one exception the points all fell within normal limits, showing that this is not influenced by pellagra (see Fig. 5). Further, a careful comparison suggested no correspondence between the Q–T interval and the clinical course of the pellagra process.

As regards the rate of the heart, sinus tachycardia was often encountered,

as may be seen from Tables I and II. During the period of convalescence we found remarkable bradycardia four times (Cases 7, 19, 20, and 22).
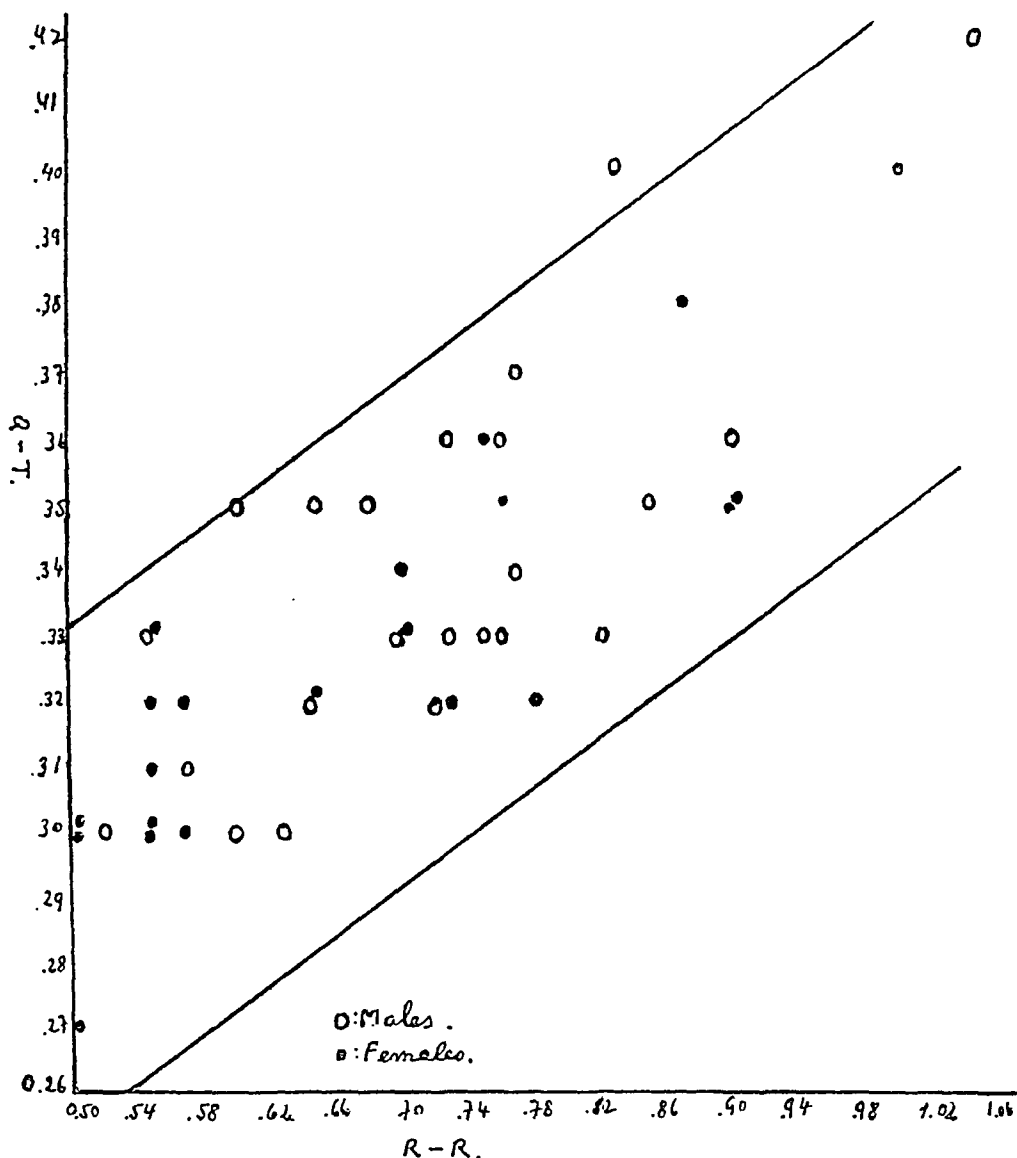
FIG. 5.—Comparison of the electric systole of the heart (Q–T interval) with the heart rate (R–R interval).

COMMENT AND DISCUSSION

In contrast to the clinical picture, in· which disturbances of the cardiac function play no important rôle, the electrocardiogram is often changed in pellagra. Abnormalities were encountered in about two thirds of our pellagrins whose cardiac condition was clinically normal.

That there is a close association between these findings and the pellagra process is shown by the marked parallelism between the clinical development of the disease and that of the electrocardiogram. It is shown by the fact that the cardiogram sometimes returns to normal when the clinical condition

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is cured. Like Feil (1936) and Smith *et al.* (1937) we are in a position to furnish an example. Also two cardiograms that were borderline between the normal and the abnormal became normal as the cure of the pellagra advanced. The reverse, too, i.e. the appearance or accentuation of the pathological character of the cardiogram when the pellagra process deteriorates, is frequently observed.

The changes that were most frequently observed, which in view of the above arguments may be attributed to pellagra, are :

(1) low voltage (without œdema),
(2) notching of the ventricular complex,
(3) deformation of the S–T interval and negativity of the T wave,
(4) shortening of the P–R interval in some cases.

We also observed sinus tachycardia at the climax of the disease and sinus ' bradycardia during the period of convalescence.

Other disturbances observed by Feil, namely, the Pardee-type of T and changes of the duration of the Q–T interval, were not detected in our material.

It is interesting to compare these changes in pellagra with the cardiographic findings in beri-beri. Since in beri-beri circulatory phenomena are mostly present, more thought has been given to the cardiogram in this disease than in pellagra and a number of reports have been published on the subject (Scott and Hermann, 1925 ; Aalsmer and Wenckebach,1929 ; Keefer, 1936 ; as well as Weiss and Wilkins, 1936). As with pellagra, the cardiographic changes are by no means present in every patient with beri-beri, even when the heart is clinically affected ; nor are the abnormalities characteristic of the disease. In beri-beri too, as a rule, tachycardia is encountered and the bradycardia, which has been observed by us during the period of convalescence of pellagra, has been found with the convalescence of beri-beri also (Keefer, 1936). The morphological findings described in beri-beri are the following : decrease and notching of the ventricular complex, deformation of the S–T interval and inversion of the T wave, lengthening of the electric systole (the Q–T interval) : the same findings are, therefore, encountered in varied conditions resulting from a disturbed function of the heart muscle. That there is, however, actually a relationship between the symptoms described and beri-beri is shown by their disappearance when the clinical symptoms subside. The shortened conduction, time P–R, may be called a rather characteristic feature, since it does not often occur in connection with a disturbed muscular function. Aalsmer and Wenckebach (1929), who found the electrocardiogram of the beri-beri heart to be normal in the other respects (apart from that of the final stage), particularly stressed this peculiar disturbance. Keefer (1936) found it three times among his observations.

In our material we twice encountered a shortening of the P–R interval to below 0·12 sec. Feil (1936) also observed two cases of this type, in which the conduction time increased again with convalescence. This sign seems to us to be of particular significance.

During the last three years investigations have made it clear that the disturbances of the skin, digestive tract, and central nervous system that are found

in pellagra are brought about by a deficiency in nicotinic acid. It would be rather rash to explain all symptoms of pellagra as due to this factor. The simultaneous occurrence of the various components of the vitamin B complex in nature brings it about that an insufficient supply of vitamin B involves, in man, a variety of factors, although in any one case clinical deficiency of one or the other is the most striking feature. Quite a number of findings support this assumption. Spies and Aring (1938) found that peripheral neuritis in pellagra could not be cured by nicotinic acid, but was cured by thiamin. Spiess *et al.* (1938), moreover, observed that in some cases of pellagra nicotinic acid treatment becomes less effective if continued, and must then be supported by lactoflavin treatment. Lehmann and Nielson (1939) recently reported a case, in which during the patient's stay in hospital with an adequate diet pellagra developed immediately after beri-beri had been cured with thiamin.

The occurrence of the above cardiographic abnormalities rather frequently in pellagra is not sufficient to conclude that they are caused by deficiency of nicotinic acid. However, the rapid disappearance of these abnormalities subsequent to nicotinic acid treatment gives strong support of this assumption. The occurrence of a phenomenon, rather characteristic of beri-beri (shortening of the conduction time), in the cardiogram of some pellagrins justifies the assumption that, similarly to the peripheral neuritis in pellagra, this symptom is brought about by the deficiency in vitamin B_1.

SUMMARY AND CONCLUSIONS

Forty-five electrocardiographic records of 23 pellagrins with normal circulatory condition have been studied.

In about three fifths the cardiogram was abnormal. That these abnormalities have a causal relationship to pellagra is demonstrated by the fact that their development is parallel to the clinical course of the disease, and particularly by the rapid disappearance of these changes in some cases subsequent to nicotinic acid treatment.

Tachycardia is mostly encountered at the climax of the disease and bradycardia during the period of convalescence.

The most frequent changes in the electrocardiogram are :

(1) low voltage of the ventricular complex,
(2) notching of the ventricular complex,
(3) deformation of the S–T interval and inversion of the T wave, and less commonly
(4) shortening of the P–R interval.

These changes are, however, not in themselves characteristic of pellagra. Since Aalsmer and Wenckebach (1929) consider this last characteristic of beriberi, it must be assumed that in pellagra also it may be brought about by a deficiency of vitamin B_1, accompanying the deficiency of the pellagra-preventive-factor.

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THE EFFECT OF ELECTRODES MADE OF DIFFERENT METALS ON THE SKIN CURRENTS

BY

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The use of metal electrodes combined with some form of conducting jelly has become almost universal in recent years, largely on account of their convenience over the former non-polarizable type of electrodes, and also to a lesser degree owing to the more frequent use of lead IV. The metal used in the construction of the electrode itself varies considerably and we think that the importance of choosing the most suitable metal for these electrodes has not been sufficiently realized, especially when using one of the older types of electro-cardiograph machines in which the skin current is neutralized by means of a compensating current, i.e. not the modern condenser model.

Attention was first drawn to the large skin currents that were produced, when a new series of electrodes was constructed for recording lead IV. All these electrodes were of equal size and consisted of brass discs, 1·125 in. in diameter ; they were all chromium-plated in order to improve their appearance. When tried on a patient, it was found, however, that the skin current varied considerably ; and also that if there was, with one pair of electrodes, a very large skin current in one direction, the current flowed with equal intensity in the opposite direction when the electrodes were reversed ; this showed that the skin current was produced by the electrode itself and was not dependent upon any peculiarity of the patient. The skin currents were frequently so large that it was impossible to neutralize them by the compensating current.

A rough test with the chromium-plated electrodes showed that when a cloth, moistened with jelly, was placed between certain pairs of electrodes there was a considerable current that varied with individual electrodes : the direction of the current could be reversed by reversing the electrodes. When brass electrodes were used, less current was produced as a rule, but the amount was still considerable.

A number of experiments were carried out to investigate this variability in the skin currents with electrodes made of different metals, and also the changes that took place with electrodes made of the same metal.

The following materials were tried : (1) brass ; (2) German silver ; (3) tin-coated brass ; and (4) tin.

Voltaic E.M.F. due to the Electrodes

The electrodes were tested by putting them on a moistened cloth, which rested on a brass plate, and the arrangement for making the tests is shown in Fig. 1. Two solutions were employed for soaking the cloth :

(1) Cambridge electrode jelly ;

(2) a gum tragacanth solution containing about 25 per cent. of salt (R.I. jelly).
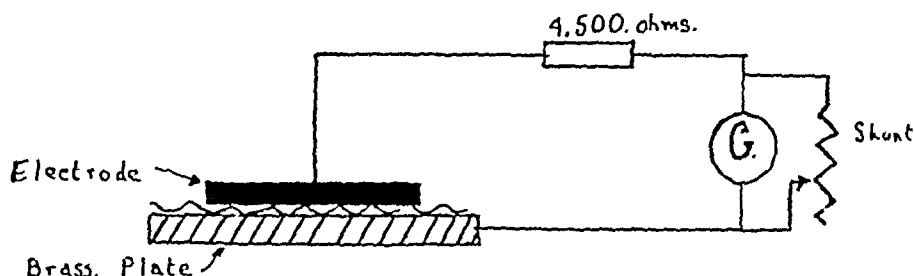
Fig. 1.—Method of testing electrode which is placed on a brass plate and separated from it by a layer of moistened cloth.

The results are given in Table I, and the last column shows the number of millivolts between a brass plate and the electrode, due to the solution employed for soaking the cloth. This was estimated from the current passing

TABLE I

E.M.F. developed with Electrodes of Different Metals

Type of Electrode	Electrolyte	Millivolts
Brass No. 1	R.I. Jelly	11·1
Brass No. 2	R.I. Jelly	2·4
German silver No. 1	R.I. Jelly	135
German silver No. 2	R.I. Jelly	137
German silver No. 1	Cambridge Jelly	105
German silver No. 2	Cambridge Jelly	98
Tin No. 1	R.I. Jelly	150
Tin No. 2	R.I. Jelly	150
Brass (tin-plated) No. 1	R.I. Jelly	145
Brass (tin-plated) No. 2	R.I. Jelly	146

through the galvanometer and the resistance of the circuit. The electrodes were then tried in pairs, with the cloth soaked in jelly between, as shown in Fig. 2.
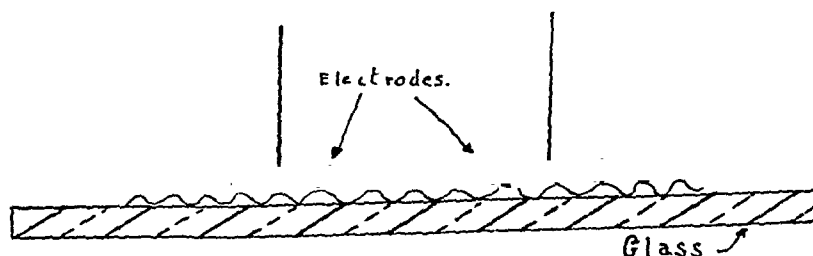
Fig. 2.—Method of testing electrodes in pairs, placed on a glass plate and separated from it by a layer of moistened cloth.

The voltage was measured between pairs of similar electrodes. In making

the tests, the electromotive force was measured after allowing the current produced by the voltaic action of the electrodes to pass for a considerable time until steady conditions had been obtained. In some cases it was noticed that the current did not reach a steady value until three or four minutes after the connection had been completed, the current generally increasing to a steady value. Two brass electrodes, cut from the same piece of thin brass, showed a large difference in the voltaic electromotive force, which was apparently due to slight differences in the composition of the brass. Chromium-plated electrodes also gave variable results, which appeared to be due to slight irregularities in the chromium-plating. German silver electrodes of one type gave fairly satisfactory results, but these were not uniform and depended upon the nature of the alloy used for the German silver. It was suggested that tin electrodes might be used and these were found to be very satisfactory. It will be noticed that the voltage between a tin electrode and the brass plate (Table I) is considerably higher than with some of the other metals. The difference between the E.M.F. due to each of the two tin electrodes, however, is less than it is between any of the other pairs of electrodes. These results are shown in Table II :

<div align="center">

TABLE II

E.M.F. BETWEEN PAIRS OF ELECTRODES

</div>

Type of Electrode	Electrolyte	Millivolts
Brass No. 1 and 2	Cambridge Jelly	8·4
Brass No. 1 and 2	R.I. Jelly	4·1 to 8·4*
German silver No. 1 and 2.. ..	Cambridge Jelly	7·0 to 12·0
German silver No. 1 and 2.. ..	R.I. Jelly	1·5 to 2·6
Tin No. 1 and 2	R.I. Jelly	<1·0
Brass (tin plated) No. 1 and 2 ..	R.I. Jelly	0·6 to 2·5*

<div align="center">

* After rubbing.

</div>

There is, therefore, a smaller " electrode effect " with tin electrodes than with the other metals. The variations in zero observed on the cardiograph are negligibly small with tin electrodes and do not change to any appreciable extent during the taking of a cardiogram. Although tin was found to be the most satisfactory metal from this point of view, the voltaic E.M.F. between it and brass is very considerable, and it seemed likely that a more inert metal, like lead, might be used with advantage. The difficulty, however, with lead is that the surface tends to oxidize and requires frequent cleaning if good contact is to be made with the skin.

<div align="center">

APPARENT RESISTANCE BETWEEN ELECTRODES THROUGH CLOTH SOAKED IN JELLY

</div>

There was found to be a considerable difference, with the different electrodes, in the electrical resistance between the electrode and a brass plate with cloth soaked in jelly to separate them. The electrodes were, as before, circular discs, 1·125 in. in diameter. This resistance was due apparently to a surface resistance effect. The results are shown in Table III and were measured with the arrangement shown in Fig. 3. The voltaic E.M.F. produced by the electrode was used

to send current through the galvanometer, and two readings were taken—one with the galvanometer alone and the other with a millivoltmeter of 500 ohms resistance shunted on it. With this arrangement it is easy to calculate the effective resistance between the electrode and the brass plate. The differences are very large, the tin and tinned brass giving much the lowest values. The increased resistance would seem likely to be due to the formation of films on the surface of the electrodes, which offer a large resistance to the passage of the current in the case of brass and German silver.

TABLE III

RESISTANCE BETWEEN VARIOUS METAL ELECTRODES AND A BRASS PLATE

Type of Electrode	Electrolyte	Approximate Value of Resistance in Ohms.
Brass	R.I. Jelly	230
German silver (1)	R.I. Jelly	4,000
German silver (2)	R.I. Jelly	12,000
Tin	R.I. Jelly	90
Tinned brass	R.I. Jelly	80
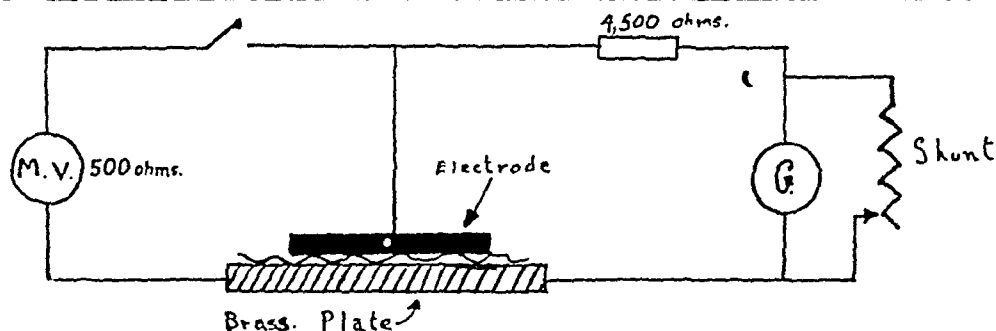
FIG. 3.—Method of measuring resistance between the electrode and a brass plate separated by a moistened cloth.

The jelly that has been used in our latest work was similar to the R.I. jelly mentioned previously with the addition of powdered pumice stone; it consisted of :

Sodium chloride	30 g.
Powdered tragacanth	3 g.
Powdered pumice stone	1 g.
Water	85 c.c.

SUMMARY

(1) These experiments show the value of tin electrodes in diminishing the amount of the skin currents, and suggest that tin is the most satisfactory material for electrodes.

(2) The superiority of tin electrodes did not appear to be due to the fact that they gave a smaller skin current than the others, but rather to this current being much more constant than with the other metals ; in consequence when two electrodes were paired the two currents balanced each other.

(3) The surface resistance of tin electrodes is smaller than that of the other metals.

(4) Almost equally good results can be obtained with brass electrodes that had been heavily tin-coated ; as these are more easily made and less expensive than the pure tin, they are now being used almost exclusively.

THE P-R SEGMENT IN HYPERTENSIVE HEART DISEASE

BY

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A recent paper (Hahn and Langendorf, 1939) on changes in the P–R segment emphasized that signs we considered typical of left auricular stress were mostly absent in arterial hypertension. On the contrary those representing right auricular stress, i.e. lowering or sloping of the P–R segment in leads II and III, often occurred. To investigate this unexpected result 200 electrocardiograms of cases with hypertension were analysed. These were selected from the records of my former Heart Clinic at Teplitz-Schoenau, Bohemia. They were recorded by the Siemens amplifying apparatus from out-patients with uncomplicated arterial hypertension, chronic glomerulonephritis, or aortic valvular disease; 160 mm. was taken as the lower limit of the systolic blood pressure and the lowest of several readings was used. There were 99 men and 101 women with an average age of 51 years and an average systolic blood pressure of 187 mm.

In the above paper we considered the displacement of the P–R segment below the iso-potential level as pathological when it reached or surpassed 0·5 mV. or when, without regard to the degree of the depression, it presented a pathological shape, i.e. a sharp rise of the P–R segment from the descending limb of the P wave followed by an arch with upward convexity (Fig. 1A, lead I ; Fig. 2A, lead I ; and Fig. 2D, lead II).

RESULTS

A pathological depression of the P–R segment was found in 148 cases, i.e. 74 per cent. In our previous paper 500 unselected cardiograms showed 24 per cent. with such changes. Its frequency in arterial hypertension is, therefore, striking. The distribution of the changes of the P–R segment according to the leads will be shown in Table I.

Examples for the various changes of the P–R segment in the different leads follow. Fig. 1 shows three cases of left ventricular preponderance with a depressed P–R segment in one lead only : the shape of the displaced segment, Fig. 1A, represents the pathological shape, i.e. a sharp rise of the P–R segment of the descending limb of the P wave followed by an arch with upward convexity.

This displacement does not seem to depend on the size of the P wave.   Fig. 2 gives cases with altered P–R segments in two or three leads.   In Fig. 2A there is a distinct discordance of the P–R segment in leads I and III as we described as typical in cases of " P mitrale " (Winternitz).
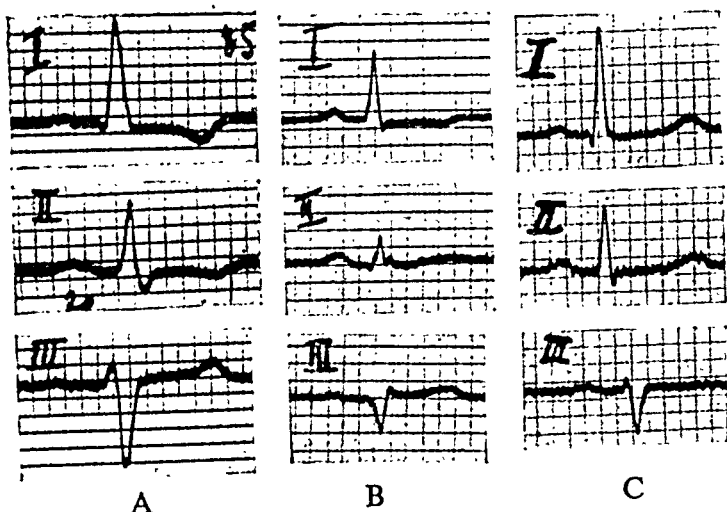
FIG. 1.—Depression of the P–R segment in one lead only, in cases of arterial hypertension. (A) in lead I, (B) in lead II, and (C) in lead III. Note the distinct left preponderance.
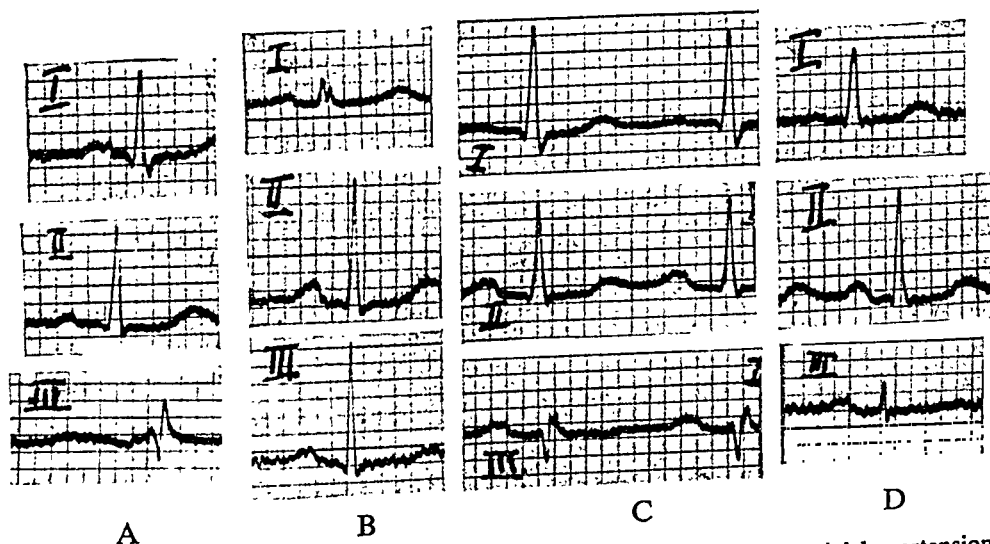
FIG. 2.—Depression of the P–R segment in several leads, in cases of arterial hypertension. (A) in leads I and II ; note the discordance of P_1 and P_3 : (B) in leads I, II, and III : (C) and (D) in leads II and III.

Table I proves that pathological changes of the P–R segment principally concern leads II and III ; 43 per cent. of the entire series and 56 per cent. of all cases with displacement of the P–R segment showed the depression in these leads. By its average age of 56 years this group exceeded that of the group with changes in leads I or I and II; and the average age of all cases

showing changes of the P-R segment was slightly higher than of those with an iso-electric P-R segment. The average systolic blood pressure presented an almost identical value.

TABLE I

Depression of the P-R Segment in 200 Cases of Arterial Hypertension

Lead	Percentage	M.	F.	Average B.P.	Average Age	Ratio of L.V.P. to R.V.P.
I and II	8·5	10	7	189	50	2·0 : 1
II II and III	9·5 43·5	15 34	4 53	195 185	56 56	1·7 : 1 1·3 : 1
I, II, and III	12·5	9	16	183	55	2·0 : 1
Total	74	68	80	187	55	—
No depression of P-R segment	26	31	21	188	50	0·6 : 1

DISCUSSION

The frequency of these changes of the P-R segment in arterial hypertension might lead us to attribute them to left auricular stress, in agreement with the conception of Wood and Selzer (1939), who found a widened P wave of low voltage, usually bifid or flat topped, in hypertensive heart disease. They attributed the changes to left auricular stress with left ventricular failure. The application of this interpretation is opposed by the fact that the most frequent alteration of the P-R segment takes place in leads II or II and III, and not in leads I or I and II, as is usual in " cor mitrale." The small group with depression of the P-R segment in leads I and II does contain proportionately numerous cases of ischæmic disturbances of the heart muscle resulting in left ventricular failure and subsequently left auricular stress—two cases of previous coronary thrombosis, one of bundle branch block, and two of severe mes-aortitis with aortic incompetence.

To ascertain if there is any relation between the incidence of this depression of the P-R segment and the heart size, the transverse diameter of the heart and the proportion with left ventricular preponderance in the groups with or without changes of the P-R segment were determined. The former showed an average diameter of the heart of 13·2 cm. and the latter of 13·5 cm., so there was no evidence of any relation between the incidence of these changes and cardiac enlargement. On the other hand, the incidence of left preponderance was much greater in the group with changes of the P-R segment than in those who showed no such depression. Table I shows the ratio of those with left ventricular preponderance to those with right preponderance or with no preponderance.

This makes it unlikely that a secondary mitral incompetence caused by a

high-grade dilatation of the left ventricle in the first group (as well as the dis-displacement of the electric axis of like origin) can be the only cause. On the other hand, there was no conclusive evidence that right ventricular and subsequently right auricular stress (as in " cor pulmonale ") are concerned in causing the changes of the P–R segment. A combination of hypertensive heart disease with emphysema or sclerosis of the pulmonary arterioles or kyphoscoliosis occurred in both groups with about the same frequency.

We were more successful in comparing the clinical features in both groups. First, there was a small difference in the average age, and of greater importance, in the structure of ages of both groups. This is well shown in Table II.

TABLE II

AGE INCIDENCE IN THE GROUPS WITH AND WITHOUT CHANGES OF THE P–R SEGMENT

Age	Cases with Changes of P–R Segment		Cases without Changes of P–R Segment	
	Number	Percentage	Number	Percentage
10–20	2	1 ⎫	0	0 ⎫
21–30	5	3 ⎬ 6	3	6 ⎬ 26
31–40	4	2 ⎭	10	20 ⎭
41–50	28	19 ⎫	7	14 ⎫
51–60	57	38 ⎬ 57	21	42 ⎬ 57
61–70	43	29 ⎫	8	16 ⎫
71–80	7	4 ⎬ 34	1	2 ⎬ 18
81–90	1	1 ⎭	0	0 ⎭
Total	147		50	

In the first group 34 per cent. were over 60 and only 6 per cent. were under 40, but in the second group only 18 per cent. were over 60 and 26 per cent. were under 40 years of age.

The second characteristic of the group with changes of the P–R segment was the frequency of ischæmic heart disease ; there were 4 instances of previous coronary thrombosis and 7 of bundle branch block. On the other hand, in the group without changes of the P–R segment we found no case of those complications. As to the prognostic value of the changes of the P–R segment a small number of out-patients only admit of very cautious conclusions, but 6 fatal cases occurred in the group with changes of the P–R segment and only 2 (that is cases of chronic glomerulonephritis) in the other group. To obtain a more convincing picture of the clinical condition of the heart muscle a series of 100 cases with different types of ventricular failure or with symptoms of cerebral sclerosis, has been analysed with regard to the P–R segment and the results are shown in Table III on the next page.

The table shows that 78 per cent. belonged to the group with changes of the P–R segment, and that on the whole they were more seriously ill than the others.

TABLE III

INCIDENCE OF CHANGES IN THE P-R SEGMENT IN VARIOUS CLINICAL CONDITIONS

Clinical Diagnosis	Cases with Changes of the P-R Segment	Cases without Changes of the P-R Segment
Orthopnœa and severe effort dyspnœa ..	24	8
Paroxysmal cardiac dyspnœa	10	2
Angina pectoris	16	8
Basal pulmonary congestion	5	4
Cerebral and other peripheral sclerosis ..	6	2
Right ventricular failure	31	4
Total (percentage)	78	22

This clinical study seems to correlate the changes of the P–R segment in hypertensive heart disease to the insufficiency of blood supply of the auricles, caused by progressive sclerosis of the auricular arteries. It is difficult with the history only to determine the onset of hypertension in any one case, but the age of the patient may give a hint. Generally the arteries of the older patients have been exposed for a longer period to a high blood pressure with its well-known consequences in producing arteriosclerosis. Pathological experience shows an increase of arteriosclerosis of all organs, the heart in particular, as age advances. Clinically and pathologically, hypertension represents a common ætiological factor in coronary thrombosis ; so Conner and Holt (1929 and 1930) found arterial hypertension in 34 per cent., Parkinson and Bedford (1928) in 49 per cent., and Levine (1929) in 40 per cent. of cases. Thus we may suggest an inadequate coronary blood flow as the most probable cause for the changes described.

SUMMARY

1. In 200 electrocardiograms from cases of arterial hypertension, depression of the P–R segment, reaching or exceeding 0·5 mV., was found in 74 per cent. of the whole series ; in 53 per cent. in lead II or in leads II and III.

2. The average systolic pressure was the same in those with and in those without these changes.

3. The average age of those with these changes in the P–R segment was rather older, and 34 instead of 18 per cent. were over 60 years of age.

4. There was a larger proportion with left ventricular preponderance.

5. The clinical condition of the heart was rather more severe in the group with these changes.

6. It is suggested that the changes of the P–R segment in hypertension result from arteriosclerosis of the auricular arteries, causing an insufficient blood supply of this part of the heart muscle.

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THE SYNDROME OF SHORT P–R INTERVAL, APPARENT BUNDLE BRANCH BLOCK, AND ASSOCIATED PAROXYSMAL TACHYCARDIA

BY

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In 1930, Wolff, Parkinson, and White published the first collected series of eleven patients, who were apparently healthy but had electrocardiograms suggesting bundle branch block combined with a shortened P–R interval. Most of them were subject to attacks of paroxysmal tachycardia and a few to paroxysms of auricular fibrillation. Isolated cases of this nature had been reported by Wilson (1915), Wedd (1921), and Hamburger (1929). Numerous authors since 1930 have added to the published cases and considered the mechanism of the syndrome. Our purpose is to review present opinion, to report further cases, and to examine the various hypotheses advanced in explanation.

The electrocardiographic features are as follows. With a rate that is normal, P is upright, and the iso-electric segment from the end of P to R is abolished, so that the ventricular complex starts immediately after P or even overlaps the end of it, reducing the distance from the onset of P to the onset of R (the P–R interval) to less than 0·12 sec. The ventricular complex resembles that of bundle branch block ; it is widened beyond 0·10 sec., often slurred in its ascent, and notched near its summit. The R–T period may be depressed or elevated, seldom assuming the full diphasic character of ordinary branch block. A surprising fact is that these patients may at other times show a normal electrocardiogram (Fig. 1), or even alternating normal and abnormal complexes without any change in rate (Fig. 2). The records during the paroxysms of tachycardia are generally of supraventricular type.

Of these three important features—a short P–R interval, ventricular complexes of bundle branch block type, and paroxysmal tachycardia—the first is a constant finding, the second may be absent in certain cases that are included on other grounds, and the third occurs in the great majority.

The lability of the *Sh.P–R : B.B.B.** rhythm should not lead to confusion with paroxysmal bundle branch block (Comeau, Hamilton, and White, 1935 ; Bishop, 1935) in which there is a normal P–R interval, an abnormal QRS only

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* Abbreviations are not free from criticism, but in this case it seems reasonable to the authors and editor to use *Sh.P–R : B.B.B.* for the short P–R interval with bundle branch block complexes.
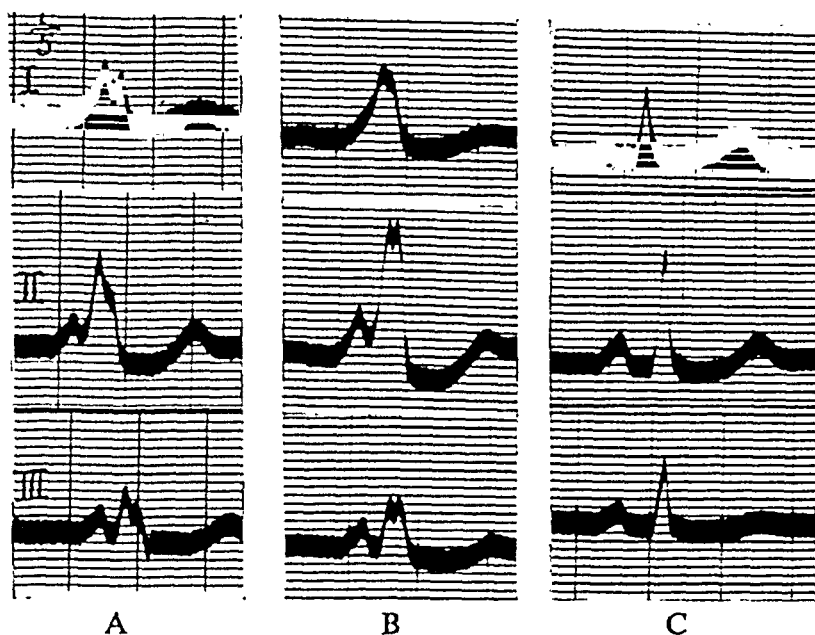
FIG. 1.—Electrocardiograms appearing spontaneously at different times in Case 1.
(A) and (B) *Sh.P–R : B.B.B.* of different aspects.   (C) Physiological.
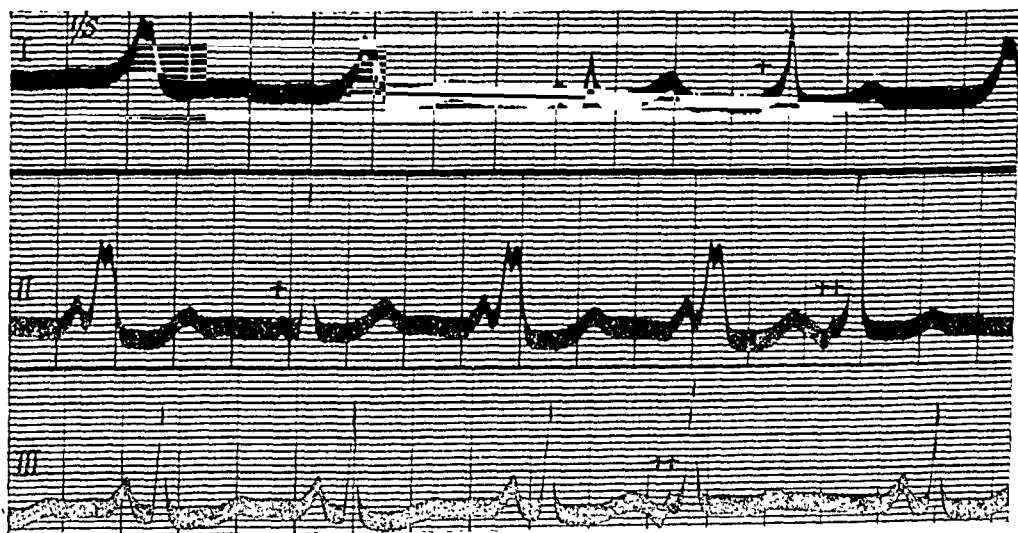
FIG. 2.—Electrocardiogram of Case 1, showing bundle branch block and physiological com-
plexes occurring spontaneously.   In addition, nodal beats (+) appear in leads I and
II, and nodal extra-systoles ($^{+}_{+}$) in leads II and III.

above a certain ventricular rate, an associated myocardial defect, and an absence
of paroxysmal tachycardia.

METHOD OF INVESTIGATION

The series comprises 22 patients of whom 19 show the fully developed
syndrome of *Sh.P–R : B.B.B.*, while the remaining 3 show a *Sh.P–R* interval
only, and are included because they are related.   The general incidence of the

syndrome, the state of the heart, the frequency and duration of the paroxysmal attacks, and the prognosis were investigated clinically. The conditions influencing the reversion of the electrocardiogram from the *Sh.P-R : B.B.B.* type to the physiological type were studied by graphic methods, especially in six favourable cases.

CLINICAL ANALYSIS

Incidence.—The full *Sh.P-R : B.B.B.* syndrome is uncommon, for a search has found no more than 90 reported cases ; the largest series was that of 11 cases by Wolff, Parkinson, and White (1930). With the 19 cases of our own, the total now reaches about 109. The rarity of the syndrome is also apparent from the fact that among 19,000 electrocardiograms in the Cardiac Department of the London Hospital the syndrome was found only three times ; and among 14,000 in a consulting practice only eight times. These 8 cases constitute 5·7 per cent. of 140 consecutive bundle branch block cases, and 5·3 per cent. of 150 consecutive cases of paroxysmal tachycardia. The only symptom that may be attached to the syndrome is the occasional palpitation due to paroxysmal tachycardia. Otherwise it is only recognized on routine electrocardiographic examination. If paroxysmal tachycardia does occur, several examinations at other times may be necessary for its recognition, as a normal cardiogram does not exclude the appearance of *Sh.P-R : B.B.B.* on other occasions. It is thus likely that some cases escape recognition. The youngest recorded in our series is 16 years ; the case of a boy aged 4 years has been described (Hamburger, 1929), and that of another boy of 14, who had been subject to paroxysmal tachycardia since he was 2 years old (Wolferth and Wood, 1933). Our oldest patient is 59, and the oldest reported is 62 years.

Associated Heart Disease.—The statement made by Wolff, Parkinson, and White (1930) that the syndrome affected people who were otherwise healthy was supported by nearly all subsequent writers, although in fact 18 of the 90 reported cases had signs of heart disease that was regarded as incidental (Wolferth and Wood, 1933 ; Cossio, Berkonsky, and Kreutzer, 1936 ; Holzmann, 1937 ; Fernbach, 1937 ; Hartog, 1938 ; Fischer, 1938 ; Gruber, 1938). These included hypertension, mitral stenosis, aortic incompetence (syphilitic and rheumatic), and coronary thrombosis. In 6 of these 18 there is reason to think that the heart disease had some bearing on the occurrence of the syndrome. Fulchiero (1935), Katz and Kaplan (1938), found *Sh.P-R : B.B.B.* after coronary thrombosis. In the thyrotoxic patient of Master, Jaffe, and Dack (1937) the *Sh.P-R : B.B.B.* disappeared after thyroidectomy. Bain and Hamilton (1926) recorded a characteristic curve in a case of rheumatic carditis without any valvular lesion. In one of Gruber's (1938) patients the abnormality was detected during a severe throat infection ; and a patient of Wilson's (1934) showing it died during a prolonged paroxysm of tachycardia, and necropsy revealed myocardial changes.

In our series only three showed certain signs of organic heart disease (Table I). The first paroxysm immediately followed a first attack of rheumatic fever

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in a patient with aortic incompetence (Case 7) ; it came 15 years after such an attack·in another with aortic incompetence and mitral stenosis (Case 10). A third never had paroxysms, but he first showed the characteristic electrocardiogram immediately after an attack of rheumatic fever that did not otherwise affect his heart (Case 12). One had hypertensive heart failure, but never paroxysmal tachycardia (Case 13). Another had no other abnormal heart signs when examined, yet according to his doctor he died one year later of congestive heart failure (Case 15). A sixth had his first paroxysm during lobar pneumonia (Case 17), a seventh had a positive Wassermann (Case 18), and an eighth with a short P–R interval only and no paroxysmal attacks had thyrotoxicosis (Case 22). Two others had a double first sound (Cases 19 and 20). Thus in about a third of our series some evidence of myocardial damage was obtained, but as no full necropsy reports are yet available, its importance cannot be assessed. Ordinary paroxysmal tachycardia with a normal cardiogram between attacks is comparable in that the patient is generally free from detectable organic heart disease, though in a proportion it does result from cardiac damage.

TABLE I

CLINICAL FEATURES OF PATIENTS WITH *Sh.P–R : B.B.B.* SYNDROME

Case No.	Sex and Age	Time in years		Duration of Paroxysms	Remarks on Heart*
		Under Observation	Liability to Paroxysms		
1	F. 54	5	26	2–4 hours	—
2	F. 17	6	2	2–48 hours	—
3	M. 19	3	—	—	—
4	F. 51	6	18	1–8 hours	—
5	F. 37	14	—	—	—
6	F. 48	1	31	1–7 days	—
7	M. 51	1/12	36	12–24 hours	Rh.A.I.
8	M. 49	4	11	up to 5 days	—
9	M. 35	11	16	minutes	—
10	M. 24	1/12	1/12	1 day	A.I. and M.S.
11	F. 20	8/12	5	15–30 min.	—
12	M. 16	10	—	—	R.F.
13	M. 58	1/12	—	—	B.P. 240/130
14	F. 35	4	3	3 hours	—
15	M. 54	1	20	1–12 hours	Died
16	M. 45	1	27	1–8 hours	—
17	M. 44	8	3	30 min.	Pneumonia
18	M. 53	5/12	2	8 hours	W.R.++
19	M. 47	14	30	minutes	†
		Short P–R and Normal Ventricular Complexes			
20	M. 33	8/12	2	5–30 min.	†
21	F. 35	Once	—	—	—
22	F. 41	Once	—	—	Th.

* Except as stated in the last column, there were no symptoms or signs of cardiovascular disease apart from those of the syndrome ; see text above for explanation of the symbols.
† Double first sound.

Liability to Paroxysms.—This is greater in patients with *Sh.P–R : B.B.B.* than in those with *Sh.P–R* only. Four of the former group and two of the

latter group gave no history of paroxysms. There is some evidence that the presence of associated heart disease makes paroxysmal tachycardia less likely. Two of the four examples of *Sh.P-R : B.B.B.* without paroxysms were Case 13 with hypertensive heart failure and Case 12 with *Sh.P-R : B.B.B.* consequent upon a rheumatic attack. The three cases described by Fulchiero (1935), by Master, Jaffe, and Dack (1937), and by Katz and Kaplan (1938), with severe myocardial damage were similarly free from paroxysms. On the other hand, two of our series (Cases 3 and 5), like two others reported by Newman (1931) and by Eckey and Schäfer (1938), had no other evidence of heart disease and yet they were not subject to paroxysmal tachycardia. Incidentally, the paroxysms in patients with *Sh.P-R : B.B.B.* seem to present no unusual features (Table I).

Prognosis.—This is obviously of great importance in view of the admitted seriousness of bundle branch block in general. Wolff, Parkinson, and White (1930) regarded the syndrome as benign, and all other authors have followed this view with the single exception of Wilson (1937), who saw a patient with it die in a paroxysm of tachycardia. Of our own patients—some observed for several years—one died of congestive heart failure, two had and still have valvular disease, and one could not be traced. The remainder are alive and well and free from cardiac symptoms except during the paroxysms of tachycardia, which, however, continue to recur sometimes with more and sometimes with less frequency. This confirms the original belief in its comparative innocence. Admittedly the syndrome may be produced occasionally by cardiac disease, but even here the prognosis rests upon the nature and degree of the causal lesion.

This favourable prognosis may lead to confusion with the right bundle branch conduction defect first described by Wilson, Johnston, Hill, Macleod, and Barker (1934), and later by William Evans (1937), of which the benign character has been stressed by Wood, Jeffers, and Wolferth (1935). This has nothing more in common with *Sh.P-R : B.B.B.*, which is indeed better entitled to the term benign.

ELECTROCARDIOGRAPHIC ANALYSIS

In six of the cases of *Sh.P-R : B.B.B.*, and in one of *Sh.P-R* with normal ventricular complex, the electrocardiogram was found on other occasions to be physiological. This variation was spontaneous in six cases of *Sh.P-R : B.B.B.*, in two of which it could also be produced by exertion, and in one also by atropin (1/50 gr. subcutaneously). Both exertion and atropin produced a physiological curve in one case of *Sh.P-R* with normal ventricular complex (Table II).

In four other cases, however, atropin failed, although in one of them spontaneous reversion was observed. The other tests such as unilateral or bilaterial carotid compression, deep or held respiration, the Valsalva test, and amyl nitrite failed to alter the records. Atropin proves to be an unreliable method of producing reversion, as already stated by Pezzi (1931) and others.

The gradual transition produced by atropin, when it is effective, may, however, shed light on the underlying mechanism.

TABLE II

PATIENTS SHOWING BOTH NORMAL AND BUNDLE BRANCH BLOCK COMPLEXES

Case No.	Change from *Sh.P–R : B.B.B.* to Normal			Shape of P	
	Spontaneous	After exercise	After atropin	*Sh.P–R : B.B.B.*	Normal
1	+	+	+	Peaked	Rounded
2	+	+	–	No difference.	
3	+	–	–	Peaked	Rounded.
4	+	–	–	No difference.	
5	+	–	–·	Both rounded but of different shape.	
18	+	–	–	Both peaked but of different shape.	
20*	–	+	+	Inverted and peaked in lead I.	Rounded and upright in lead I.

* Change only from Sh.P–R to normal P–R.

The records of Case 1 show spontaneous variations between *Sh.P–R : B.B.B.* and normal complexes (Fig. 1), and in certain portions nodal beats and nodal extrasystoles are also seen (Fig. 2). In this patient atropin was used twice. On the first occasion bundle branch block complexes similar to those of Fig. 1A were present, and 20 minutes after the injection a different branch block complex appeared, similar to those of Fig. 1B. At the same time P changed in shape (Fig. 3A), the original sharp peaked wave giving place to a broad and

A   B
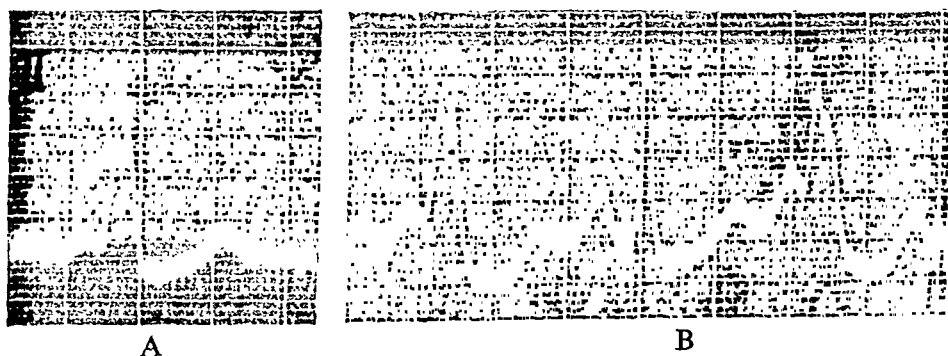
FIG. 3.—Case 1, (A) 20 minutes, (B) 50 minutes after atropin (gr. 1/50 subcut.).
(A) Complex of Fig. 1 (B) type preceded by rounded P.
(B) Complexes of Fig. 1 (B), (C), and (A) type appearing successively.

rounded one. Fifty minutes after the injection each type of complex appeared one after another (Fig. 3B). On the second occasion, two months later, complexes similar to those shown in Fig. 1B were constantly present. After atropin (25 minutes) the notch in R gradually disappeared and P assumed the rounded form of Fig. 3A ; then physiological complexes followed (Fig. 4).

Finally a gradual return to the original branch block complexes of Fig. 1B type was recorded, and it was complete 80 minutes after the injection. During
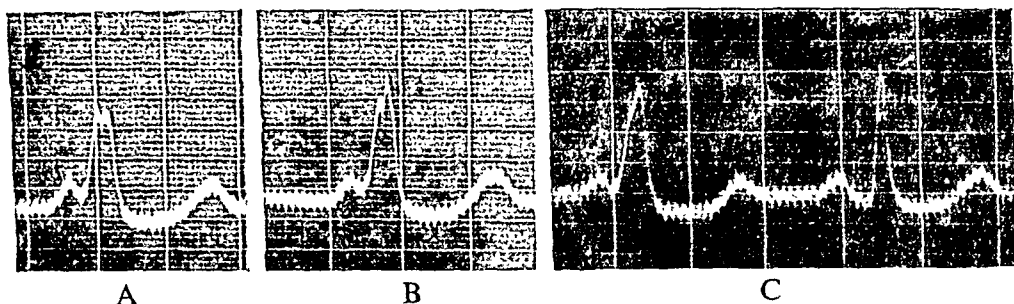
FIG. 4.—Case 1, one month later.
(A) Before, (B) and (C) 25 minutes after atropin, showing a gradual transition from *Sh.P–R : B.B.B.* (Fig. 1B type) to physiological complexes.

both experiments with atropin, nodal beats as well as nodal extrasystoles with inverted P and supraventricular complexes similar to those in Fig. 2 were often seen.

Such simultaneous changes in P and QRS occurred in Cases 3, 5, and 18, spontaneously. On one occasion complexes suggestive of an intermediate stage
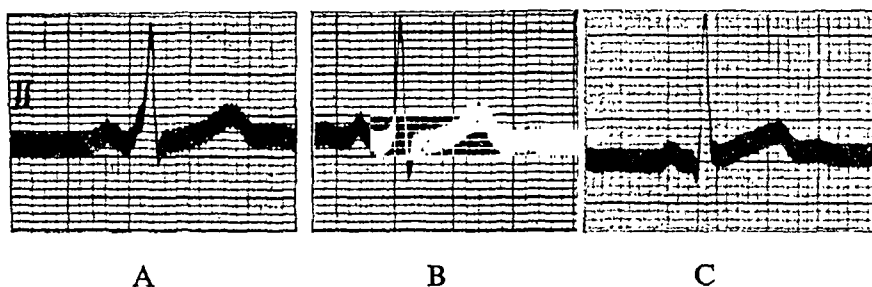
FIG. 5.—Case 3 showing spontaneously (A) *Sh.P–R : B.B.B.*, (B) transition complex, and (C) a physiological complex ; each type of complex is preceded by a different P.

between the *Sh.P–R : B.B.B.* and the physiological complexes were seen, and they were preceded by P waves of different shapes (Fig. 5).

In Case 20, an example of *Sh.P–R* and normal ventricular complex, the P wave changed shape with restoration of a normal P–R interval (Fig. 6).

These observations show that in four out of six cases of *Sh.P–R : B.B.B.* the reversion of the abnormal to the normal ventricular complex was accompanied by a change in the P wave. Under atropin, a gradual change in the shape of P accompanied a gradual change in the QRS complex (Fig. 4).

The electrocardiograms during paroxysms of tachycardia were available in seven cases. In five, supraventricular tachycardia was recorded, in one supraventricular and ventricular tachycardia, and in the remaining one auricular fibrillation and " ventricular " tachycardia.

Identification of the electrocardiogram of the syndrome rests upon the combination of a short P–R interval with a ventricular complex similar to branch block (i.e. *Sh.P–R : B.B.B.*). Where the P–R interval varies in the

different leads, difficulty may arise. In Fig. 7 the P–R interval is 0·10 sec. in lead I with a ventricular complex of 0·10 sec., while in lead II P–R is 0·16 sec. and QRS is 0·08 sec. ; in lead III also it is probably normal. To decide which limb lead gives the truest P–R indicative of auriculo-ventricular conduction, chest leads were employed. With the exploring electrode in the fifth interspace on the right sternal border and the distal electrode on the right arm, as used by Zàrday (1937) for the right auricle, we took records in six healthy students. The P–R interval in this chest lead was identical with P–R in leads II
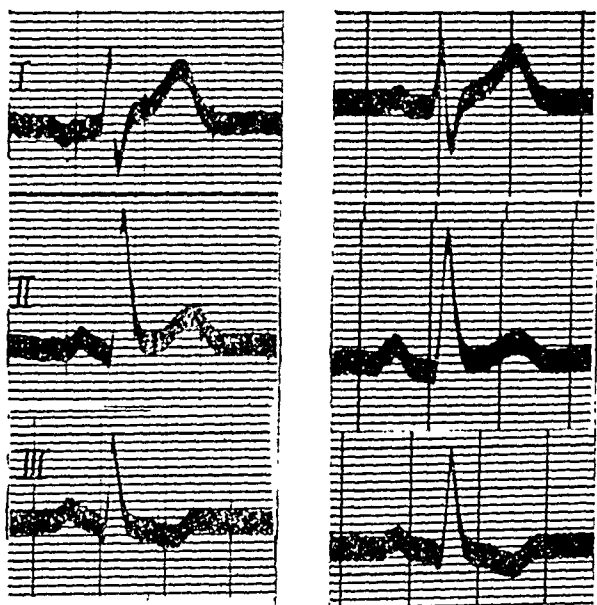
FIG. 6.—Case 20 with Sh.P–R interval only.
(A) Before and (B) 50 minutes after atropin : not on v
P₁, previously inverted, but also P₂ and P₃ change
their shape with return to normal A-V conduction.
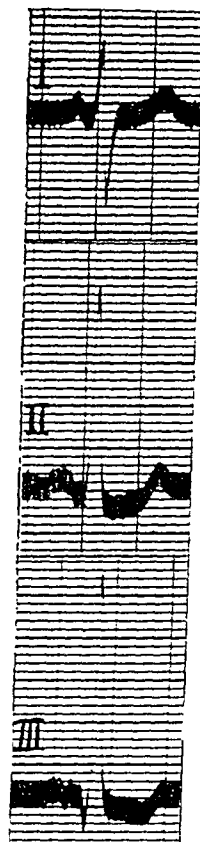
FIG. 7.
(See text.)

and III, but longer than that in lead I where the first part of P is so often iso-electric ; and as in lead III P may be inverted or diphasic, the P–R interval in lead II is the best measure of the A-V conduction. If so, the P–R interval in Fig. 7 is normal and the record is not an example of the syndrome.

In the following three (Cases 19, 8, and 12) doubt might arise whether they should be included in the syndrome or not. Although the characteristic *Sh.P–R* and modified QRS occur clearly in lead II in one (Fig. 8A), in lead I in another (Fig. 8B), and in leads I and II in the third (Fig. 8C), the other leads might be passed as normal or uncertain. Yet we have no doubt both from the general aspect of the records and from the accompaniment of paroxysmal tachycardia that all three are genuine examples of the syndrome. The

" iso-electric " P–R interval includes a slight curve (Fig. 8 A and B), or a notch (Fig. 8C) representing the initial part of the QRS complex.
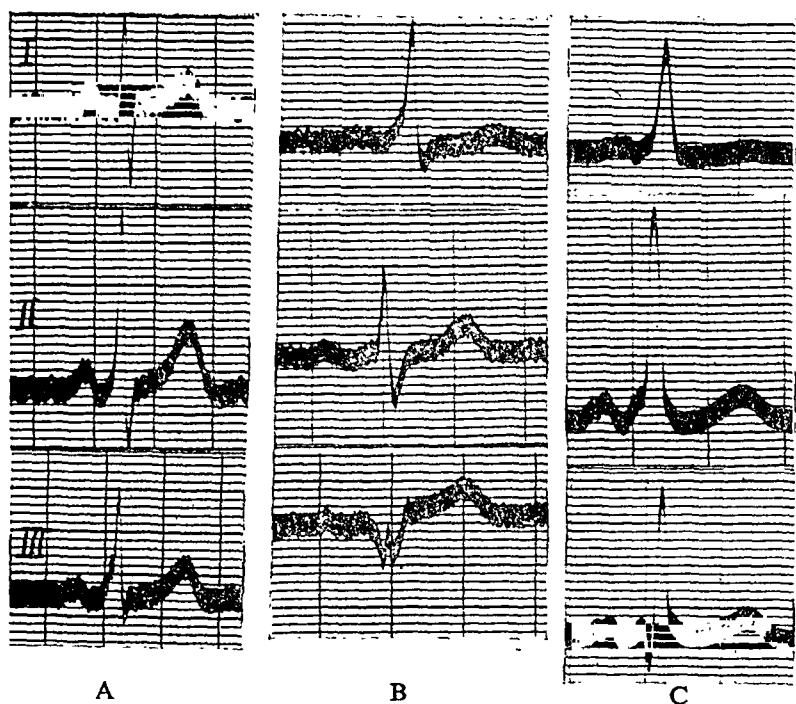
FIG. 8.—Electrocardiograms in three patients with *Sh.P–R : B.B.B.*
(A) Case 19, (B) Case 8, and (C) Case 12. The characteristic slurring with Sh.P–R interval appears in leads I and III of (A), in lead II of (B), and in lead III of (C), as a modified almost iso-electric P–R period.

PREVIOUS HYPOTHESES

No satisfactory explanation for the mechanism of the syndrome seems to have been given, no method of reproducing the abnormality in experiment is known, and no post-mortem study of any established clinical case has been published. An attempt has been made in Table III to classify the various hypotheses advanced.

Wolff, Parkinson, and White (1930) regarded it as true bundle branch block resulting from some abnormal vagal effect which at the same time accelerated A-V conduction ; in one case removal of vagal control by exercise or by atropin converted the abnormal complex into a normal one. Pezzi (1931) disagreed, maintaining that vagal release was often ineffective, and postulated a paranodal pacemaker due to an irritative lesion near the A-V node, affecting conduction to one ventricle only. Sigler (1933) reported cases in which branch block appeared when the R–T interval was shorter than a certain critical length, but normal when it was of greater length ; he therefore assumed that it represented fatigue of the conducting system. Hauss and Schütt (1938) accepted Condorelli's belief in both sino-auricular and sino-nodal pathways, and imagined a simultaneous block of the S-A pathway and of one bundle branch. Thus a *Sh.P–R* might be produced from a more direct impulse along the sino-nodal route and be accompanied by branch block.

TABLE III

CURRENT EXPLANATIONS OF BUNDLE BRANCH BLOCK WITH A SHORT P–R INTERVAL

I. *Hypotheses accepting it as True Bundle Branch Block.*
    (1) With sinus pacemaker :
        (*a*) Abnormal vagal influence (Wolff, Parkinson, and White, 1930 ; Wilson, 1915).
        (*b*) Fatigue of conductive system (Sigler, 1933).
        (*c*) Block of S-A pathway and of one bundle branch (Hauss and Schütt, 1938).
    (2) With abnormal pacemaker :
        Paranodal rhythm and block of one bundle branch (Pezzi, 1931 ; Wedd, 1921 ;
        Tung, 1936 ; Katz and Kaplan, 1938).

II. *Hypotheses rejecting it as True Bundle Branch Block.*
    (1) Ventricular asynchronism due to premature stimulation of one ventricle :
        (*a*) By bundle of Kent (Holzmann and Scherf, 1932 ; Wolferth and Wood, 1933 ;
        Scherf and Schönbrunner, 1935 ; Roberts and Abramson, 1936 ; Zàrday,
        1938 ; Holzmann, 1937 ; Fernbach, 1937).
        (*b*) By increased conductivity of A-V node and one bundle branch (Fulchiero,
        1935 ; Spangenberg, Vedoya and Gonzalez, 1937 ; Hartog, 1938).
        (*c*) By increased conductivity of one bundle branch with nodal rhythm (Pines,
        1938).
        (*d*) By mechanical excitation from the auricle of an irritative focus in one ventricle
        (Holzmann and Scherf, 1932 ; Cossio, Berkonsky, and Kreutzer, 1936).
        (*e*) By ventricular extrasystole interfering with a normal sinus beat (Moia and
        Inchauspe, 1938).
    (2) Abnormal ventricular complex due to an electrical event during the iso-electric P–R
    period :
        (*a*) Auricular extrasystole (Gruber, 1938).
        (*b*) Electrical event resulting from persistent (foetal) conducting fibres (Eckey and
        Schäfer, 1938).

That there is no true branch block is the opinion of numerous writers, especially Holzmann and Scherf (1932) and Wolferth and Wood (1933). They found that the P–T interval was within the limit of normal ventricular conduction, contrary to the rule in true bundle branch block. Further they found the same P–T interval in both normal and abnormal complexes where both were present in the same patient. In these papers it is assumed that there is an accessory pathway of A–V conduction, such as was described by Kent (1892), and that this pathway may function ; this in their opinion would easily explain the *Sh.P–R* and the premature excitation of one ventricle simulating branch block. The paroxysms of tachycardia were ascribed by Wolferth and Wood to a retrograde conduction at a favourable moment giving rise to a circus movement. Normal conduction and normal curves appeared when the sinus impulses reached a certain rate—a rate beyond the conductivity of the bundle of Kent.

Other authors have also rejected branch block as an explanation. Fulchiero (1935) and others (see Table III) suggested that there was an increased conductivity of the specific system, notably of the A-V node and of one branch of the bundle. Pines (1938) invoked a similar state in one bundle branch, but explained the *Sh.P–R* as consequent upon a nodal rhythm. Cossio, Berkonsky, and Kreutzer (1936), accepting the suggestion of Holzmann and Scherf (1932), believed that a normal auricular contraction mechanically stimulated an excitable focus in one ventricle, from which a *Sh.P–R* and also an abnormal ventricular complex resulted.

Still opposing the hypothesis of a true bundle branch block, other authors speak of an abnormal electrical activity during the iso-electric P–R period.

Gruber (1938), using auricular leads, regarded the normal P as quickly followed by an auricular extrasystole that deformed the ascending limb of R so that branch block was imitated.   Eckey and Schäfer (1938) assumed the persistence of embryonic conducting fibres in the auricles, so that the normal P was immediately succeeded by a bizarre ventricular complex.

Bearing upon the mechanism of the syndrome we have also consulted Elliott and Nazum (1932), C. Evans (1937), Sprague (1937), Ritter (1939) ; and on the electrocardiographic aspect Herzum (1934), Dressler (1937), Bishop (1937), Arana and Cossio (1938), and Campbell and Elliott (1939).   Under war conditions we have been unable to examine the paper of Teràn (1938).

DISCUSSION

Any hypothesis explaining the mechanism of this syndrome must deal first with the site of the pacemaker, and secondly with the diffusion (or conduction) of the impulse.   The fact that during a reversion of *Sh.P–R : B.B.B.* to normal the P wave often changes in shape is strongly against the view that in both conditions the impulse arises in the sinus node.   The gradual change of P coincident with gradual changes in the ventricular complex, as here described, makes the use of an accessory pathway (such as Kent's) unlikely, though that is how Holzmann and Scherf (1932), Wolferth and Wood (1933), and others have tried to explain it.   With the bundle of Kent in operation the shape of the P wave should be identical before both abnormal and normal complexes (Wolferth and Wood, 1933).   But as stated by Pines (1938) and even in the cases recorded by Scherf and Schönbrunner (1935) and by Zàrday (1938)—partisans of the bundle of Kent—changes in the shape of P on reversion to normal are evident ; and they are present in some of the records of Fernbach (1937), Chen Lang Tung (1936), Moia and Inchauspe (1938).   With an alternative route along a bundle of Kent, there should be two distinct curves and no intermediate ones, but there were intermediate ventricular complexes in the cases of Wilson (1915) and Chen Lang Tung (1936), and in four of our own.   As the P of the normal and of the branch block complex are often different, the sinus pacemaker cannot be in sole control.

Pezzi's (1931) explanation of an abnormal pacemaker near the A–V node would fit in with the change in P with change in complex.   Even an upright P in all leads does not exclude this hypothesis (Holzmann and Scherf, 1933), and the liability to paroxysms might be expected with an irritative lesion involving the A–V node.   Yet the coexistent bundle branch block can scarcely be explained in this way.

Leaving the subject of the P wave, the ventricular complex looks like a branch block, but is it one ?   The appearance has been ascribed to conduction by the bundle of Kent, to increased conductivity in one bundle branch, or to a premature excitation of one ventricle.   All three ideas connote asynchronism of the two ventricles, which is also inseparable from true bundle branch block. Ventricular asynchronism is said to be present by Wolferth and Wood (1933) Scherf and Schönbrunner (1935), and Moia and Inchauspe (1938).   Others

(Battro, Braun-Menendez and Orias, 1937 ; Spangenberg, Vedoya and Gonzalez, 1937 ; Braun-Menendez and Solari, 1939) deny ventricular asynchronism in the syndrome. Triple rhythm is an uncertain sign of asynchronism ; it was noted in only 1 of our 19 cases, an infrequency contrary to the experience of Wolferth and Wood (1933).

A second objection to the existence of a real branch block is the fact that the R–T interval with change to normal complexes remains almost unaffected. In contrast the R–T interval in cases of paroxysmal branch block increases with onset of branch block by at least 0·05 sec. (Table IV). On the left are the six cases of our own where a change to normal complexes took place, and on the right one case of our own (K) and nine cases from Comeau, Hamilton, and White (1935), in which fairly exact measurements were possible.

A third objection is the difference in form between the curves of true bundle branch block and those found in this syndrome. The features of *Sh.P–R : B.B.B.* are these. The very beginning of the ventricular complex is slurred in one or more leads, though sometimes the slurring appears almost iso-electric in other leads where it looks like a normal P–R interval succeeded by a normal ventricular complex (Fig. 8). The slurring more often involves the foot of the ascending limb of R, giving the most characteristic appearance of all (Fig. 1, 5A, and 8 A, B, and C), very different from true branch block as we think. Another distinguishing feature is the form of the S–T and the T of the complex. Even when R or S is large and emphatic, it is seldom followed immediately by any big swing in the opposite direction ; indeed, a T approximating to normal is the rule. The characteristic diphasic appearance of the pathological branch block is seen only in about 10 per cent. of the *Sh.P–R : B.B.B.* cardiograms.

TABLE IV

THE R–T INTERVAL IN *Sh.P–R : B.B.B.* AND IN PAROXYSMAL BUNDLE BRANCH BLOCK

Cases of this Series			Cases of Comeau, Hamilton, and White (1935)		
	Short P–R with Bundle Branch Block			Paroxysmal Bundle Branch Block	
Case No.	R–T in Normal (sec.)	R–T in B.B.B. (sec.)	Case No.	R–T in Normal (sec.)	R–T in B.B.B. (sec.)
1	0·38	0·38	2	0·28	0·33
2	0·40	0·40	3	0·35	0·40
3	0·40	0·42	4	0·37	0·42
4	0·34	0·36	6	0·35	0·40
5	0·33	0·36	8	0·33	0·36
18	0·33	0·33	9	0·31	0·36
			10	0·37	0·42
			11	0·35	0·43
			12	0·33	0·39
			K	0·40	0·45
Average	0·363	0·375	Average	0·344	0·396

Taken together, the doubt about ventricular asynchronism, the lack of change in the R–T distance on reversion to normal, the peculiar shape of the very first part of the ventricular complex, and the rarity of the gross diphasism of ordinary branch block, invalidate the true branch block hypothesis. The last two hypotheses in Table III, like those already discussed, fail to explain the gradual change in the P wave and the ventricular complex (Fig. 4).

From our own findings we are of opinion that any hypothesis should explain the following features :

1. The difference in the shape of P before normal and *Sh.P–R : B.B.B.* complexes.
2. The peculiar shape of the ventricular complex compared with that of ordinary branch block.
3. The gradual change of P and QRS from *Sh.P–R : B.B.B.* to normal (after atropin), and the appearance of intermediate ventricular complexes (Fig. 4).

Since previous explanations did not meet these points, we began to formulate the view of a double rhythm composed of two interfering pacemakers. The idea was that a nodal beat might be superimposed upon a normal PQRST complex, so that the P–R interval was shortened by the early ventricular complex of the nodal beat, which was then succeeded by the normal ventricular complex, the two in juxtaposition giving a broad wave simulating branch block. Such a conception was encouraged when we found that a complex, such as the second in Fig. 2 (lead II), imposed upon a normal complex, such as Fig. 1C (lead II), gave a resultant complex not unlike that of the syndrome. The idea was abandoned because it is difficult to believe that two supraventricular impulses, each passing down the whole of the bundle system, could follow one another so closely in time ; the first impulse must leave behind it a refractory period which would bar the passage of the second.

Such a difficulty might be overcome by assuming that a beat arising near the normal pacemaker (for the P is altered) is interfered with by a ventricular extrasystole arising prematurely low in one bundle branch. This is not unlike the view of Moia and Inchauspe (1938) who proposed a similar " mixed " rhythm as a modification of the purely extrasystolic hypothesis of Holzmann and Scherf (1932) and Cossio, Berkonsky, and Kreutzer (1936). Graphic evidence of interference between a sinus and a ventricular beat is given by Wenckebach and 'Winterberg (1927 ; Fig. 189 D and E) though in paroxysmal tachycardia. In our view the upper impulse would spread only to the ventricle other than that producing the extrasystole. If it did so spread, it might modify the diphasism of the extrasystolic complex, especially in its S–T portion, and shorten it. Normal complexes would appear after sudden suppression of the low ventricular centre, transition complexes during its gradual suppression following vagal release by atropin. The frequency of paroxysmal tachycardia in these patients points to hyperexcitability of the conducting tissue. The absence of ventricular extrasystoles in our own cases is an objection to the kind of interference which we have suggested. Though not advancing this view as a complete solution of the

problem, the idea of a double rhythm at a normal rate, in contrast to that of true bundle branch block, seems to us the best explanation of our findings.

A short P–R interval with *normal* ventricular complex probably represents true nodal rhythm, as recognized by Pezzi (1931), Scherf and Schönbrunner (1935), and Clerc, Levy, and Cristesco (1938). It may be stable, as in our Cases 21 and 22, or unstable, as in Case 20, and it may or may not be accompanied by liability to paroxysmal tachycardia.

SUMMARY AND CONCLUSIONS

1. Nineteen patients having an electrocardiogram with a short P–R interval and a ventricular complex of bundle branch block appearance (*Sh.P–R : B.B.B.*) —the so-called Wolff, Parkinson, White syndrome—have been studied, along with three others having a short P–R interval but a normal ventricular complex.

2. The *Sh.P–R : B.B.B.* syndrome constitutes about 5 per cent. of all cases of bundle branch block (140 consecutive cases), and it is found in about 5 per cent. of patients who are subject to paroxysmal tachycardia (150 consecutive cases). About three quarters (15 out of 19) of those with *Sh.P–R : B.B.B.* had attacks of paroxysmal tachycardia, but only one of the three with *Sh.P–R* alone had attacks. The characteristic electrocardiogram may be discovered at a routine examination in persons otherwise healthy, in patients with paroxysms of tachycardia, or in those having some other cardiac disease.

3. Much as in ordinary paroxysmal tachycardia, where most patients are otherwise healthy though some have associated and even causal heart disease, so in this *Sh.P–R : B.B.B.* syndrome only a minority have organic heart disease (18 of 90 reported cases and 3 of our 19 cases). Occasionally the causal connection seems to be definite ; for instance one patient first showed the characteristic cardiogram soon after acute rheumatism ; and examples have been reported after coronary thrombosis. The prognosis seems to be unaffected by the occurrence of the syndrome, even in a patient with associated heart disease.

4. A remarkable feature is that the same patient may at one time show the typical cardiogram and at another a normal one, both at normal rates. Such switching may be spontaneous, though it may also be induced by exertion or by atropin. It is usually abrupt ; only if produced by atropin is it likely to be gradual. The paroxysms of tachycardia are generally supraventricular. Of seven patients whose paroxysms were recorded, five proved to be supraventricular, one supraventricular and at other times ventricular, and one ventricular tachycardia with auricular fibrillation.

5. A partially iso-electric P in lead I of a normal tracing with full ventricular complex (near 0·1 sec.) might simulate *Sh.P–R : B.B.B.*, except that the other leads are normal. On the other hand the slurring of R in a case of *Sh.P–R : B.B.B.* may in one lead fuse with the P–R period making it iso-electric, and like a normal beat, although the other leads are characteristic of the syndrome.

6. Bearing on the mechanism of the peculiar electrocardiogram : (*a*) P often becomes modified in shape when the abnormal cardiogram of *Sh.P–R : B.B.B.*

changes to normal, and this fact alone shows the involvement of a pacemaker that under both conditions can scarcely be a normal one ; (*b*) fixity of the R–T distance with reversion to normal, and the peculiar aspect of the apparent branch block (slurring of the foot of R and rarity of diphasism compared with true branch block) are reasons against acceptance of the syndrome as real bundle branch block.

7. As these current hypotheses scarcely explain our findings, we incline to think that the typical syndrome represents a double rhythm by two interfering pacemakers, one near the sinus and the other in one bundle branch. The modified P preceding the broad ventricular complexes is due to the upper pacemaker ; a ventricular extrasystole, arising low in one bundle, quickly interferes and so shortens the P–R interval. The aberrant QRS complex is produced by the ventricular extrasystole and is modified by the QRS of the S-A impulse which reaches the ventricle through the unaffected bundle branch. Intermediate ventricular complexes might be due to the gradual suppression of the ventricular pacemaker. The increased excitability of the conductive system (possibly congenital), responsible for the two pacemakers at a normal rate, is also indicated by the special liability to paroxysmal tachycardia. The subsidiary group, that with short P–R only, are examples of true nodal rhythm.

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ATYPICAL PAIN IN ANGINA PECTORIS AND MYOCARDIAL INFARCTION

BY

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Pain resulting from disease of the coronary arteries is characterized by its location in the chest, usually behind the sternum, and by its paroxysmal nature. In some instances, however, the pain may be entirely extrathoracic and not necessarily paroxysmal. We wish to draw attention to two groups of patients suffering from coronary sclerosis with such atypical pain. In the *first* group the pain occurs paroxysmally, is related to effort, but is *eccentrically placed* ; the attack so occasioned resembles classical angina pectoris in all other respects. In the *second* group are instances of angina pectoris and myocardial infarction in which *chronic left shoulder pain* is a prominent feature ; the latter may herald the complete attacks or follow in their wake.

GROUP 1. PATIENTS WITH ECCENTRICALLY PLACED ANGINAL PAIN

A long-recognized example of these larval or fractional forms of angina pectoris is that in which pain on effort appears only in the arms, the crucial substernal pain being absent. The true nature of such cases was recognized by Heberden (1786). One of his patients suffered from repeated attacks of pain in the left arm, on effort or at night, from 60 until his sudden death at the age of 75 ; he never experienced any chest pain. Since then many others (Mackenzie, 1923, Osler, 1910, and Allbutt, 1915) have described similar cases and commented on the diagnostic puzzle they may present. Mackenzie observed one in whom the pain was confined to the left little finger : and Allbutt one, who felt his pain in the centres of the palms of both hands on walking rapidly or on dancing ; some time later, however, he developed the full-dress type of angina and died in an attack. Osler quoted the case of Lord Clarendon, as noted by Blackall in his famous book on the dropsies, in whom the pain was always brachial, even in the fatal attack. Osler described patients where the pain was felt in the middle of both forearms or at the wrists or elbows, whose further course provided indisputable evidence of angina pectoris.

Somewhat similar, but less likely to cause confusion, is the case in which the pain commences distally and spreads rapidly towards the chest (Potain's

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angine renversée). Such pain commonly begins in the region of the wrists or elbows and may arrest the patient in his track before it has spread upwards to the chest.

Notes of our 12 cases are given in Table I and short notes of 3 of them follow.

TABLE I

PAROXYSMAL ARM PAIN, ON EFFORT, BEFORE ONSET OF CLASSICAL ANGINA

Case No.	Age	Site and Duration of Pain before Cardiac Symptoms appeared		Subsequent Course	Electro-cardiogram
1	56	Both wrists and elbows	.. 1 yr.	Typical angina, bilateral radiation	T_2, T_3 inverted
2	52	Both forearms .. .. .. 2 yr.		Cardiac infarction	T_1, T_2 inverted
3	63	Both upper arms .. .. 6 mo.		Cardiac infarction	T_2, T_3 inverted
4	50	Left arm .. .. .. 5 mo.		Typical angina, no radiation	L.A.D.
5	48	Left arm .. .. .. 4 yr.		" Angine ren-versée "	Late inv. T_1
6	63	Both wrists .. .. 2 mo.*		Not improved	Inv. T_2, T_3
7	61	Right forearm .. .. .. 2 yr.*		Not improved	Low T_2, inv. T_3
8	60	Left arm .. .. .. 8 yr.		Cardiac infarction	—
9	56	Left elbow and forearm .. 25 yr.		Cardiac infarction	Inv. T_2, T_3, T_4
10	52	Both forearms .. .. .. 4 mo.		Cardiac infarction	Low T_2, inv. T_3
11	61	Left face .. .. .. 3 yr.		Later involved L. neck and arm	T_1 inv., T_2 T_3 diphasic
12	50	Left arm .. .. .. 8 yr.		Classical angina	—

* No classical angina.

Case 1. Pain in both wrists, on effort ; typical angina 1 year later

Male, aged 56. Acute pain over flexor surfaces of both wrists and elbows, on exertion, for 2 years. No chest pain. No arthritis. Attacks relieved by rest, but sometimes last twenty minutes. More severe in left arm, with sensation as though the sphygmomanometer cuff was applied. Typical substernal angina of effort, with radiation to left arm, for one year ; relieved by nitrites. Distant heart sounds ; no cardiac enlargement. B.P. 130/80. EC., T_2 and T_3 inverted ; prominent Q_3.

Case 5. Pain in left arm on exertion ; " angine renversée " 4 years later.

An obese woman, aged 48, known to have had a blood pressure of 220 mm. at 38. Four years ago attacks of pain and " deadness " in the entire left arm, lasting a few minutes and provoked by hurry and bustle. No other symptoms till one night, after hurrying to prepare supper, she was seized with an agonizing pain in left arm, which incapacitated her. A dozen similar attacks followed in the next 24 hours and culminated in a paroxysm in which pain started in left wrist and spread slowly up to left shoulder and for the first time to the chest and substernal region. Morphia was required. The left chest was held as if in a vice. Subsequently developed classical angina, with radiation to left arm and relief with nitrites. B.P. 185/95. EC., late inversion of T_1.

Case 8. Pain in left upper arm on exertion ; classical angina 8 years later

Male, aged 60. Sharp pain in left arm above elbow and sometimes in forearm on walking briskly or on stairs for 8 years, usually with dyspnœa. No other symptoms. No physical signs and X-ray of heart and EC. normal. Two years later attacks recurred, with more dyspnœa. After another 2 years they became more frequent and severe ;

angina pectoris was suspected and nitroglycerine was at once successful. Attacks continued during the next 4 years but no substernal pain till 3 months before observation, when it started in the chest and spread down left arm. He died suddenly in hospital and autopsy confirmed an anterior myocardial infarct.

DISCUSSION

No satisfactory explanation for the referred pains of angina pectoris is forthcoming to account for all the clinical features and for some of the unexpected results of sympathectomy. According to the theory of Head and Mackenzie a stimulus passes from the heart via the sympathetic to the posterior root ganglia, where it is transformed and leads to stimulation of certain spinal ganglion cells with the appreciation of pain. This pain is felt along the distribution of the nerve root in question and so it is called referred pain. This explains the occurrence of extrathoracic pain of cardiac origin, but does not account for the inverse radiation of the pain in other instances, where it seems as if the pain *originates* in the periphery and passes towards the centre. The hyperæsthesia sometimes found with such seizures would suggest this, just as any severe peripheral pain may leave hyperæsthesia of the skin. Such patients often liken their arm pain to that produced by prolonged inflation of a sphygmomanometer cuff. Robertson and Katz (1938) maintained the sphygmomanometer cuff in position for five minutes, at a pressure 50 mm. above the systolic pressure, and found that the subsequent arm pain was followed by anginal paroxysms in 19 out of 24 patients who were subject to angina and were tested in this way. When repeated on the right arm, anginal attacks only followed if the pain radiated to that arm in the spontaneous attacks. When applied to the legs the tests failed. These results suggest that by producing *one* element of the spontaneous attack, viz. the pain in the arm, the fully developed paroxysm may be induced. By what mechanism it is brought about we do not know. On repeating these experiments we have found that, although we were unable to reproduce anginal attacks in more than half of our anginal patients, the " squeezing " or " gripping " sensations in the arm, in both the induced and spontaneous attacks, were indistinguishable. It is possible they are produced by the same mechanism, viz. ischæmia of the forearm muscles. Does spasm of smooth muscle occur in the left arm during anginal seizures ?

Penfield (1925) has shown that removal of a sympathetic ganglion takes away the possibility of angina, only in the motor distribution of that ganglion : it is still possible in the motor distribution of the remaining ganglia. He pointed out that the success of such an operation depends, not upon the interruption of a direct afferent path from cardiac sympathetic plexus to central nervous system, but upon the interruption of autonomic reflexes. Accordingly, he suggested that the nervous mechanism in angina pectoris depends on an autonomic reflex. It causes peripheral spasm of smooth muscle and may resemble the pain of various angiospastic conditions. This theory differs from Head's in that the point of contact between sympathetic and cerebrospinal systems is shifted from the posterior root ganglia to the periphery. That such an explanation is not unlikely is suggested by the replacement of pain in some

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anginal attacks by paroxysms of homolateral sympathetic stimulation (Gibson, 1905 ; Palmer, 1930 ; Holt, 1930).

The case histories outlined above emphasize the importance of studying closely any middle-aged or elderly person complaining of bouts of pain in the arm on exertion. Many such attacks, sooner or later, blossom into typical angina, but in others sudden death may occur before the coronary nature of the attacks is suspected.

GROUP II. PERSISTENT PAIN IN THE SHOULDER

A symptom that is less readily identified as due to disease of the coronary arteries is chronic pain in the shoulder and arm, not affected by exercise and not relieved by nitrites. The pain does not occur in crises, but is more persistent, lasting for hours at a time and very intractable to ordinary therapeutic measures. Howard (1930) published reports of five patients with a stiff painful shoulder in association with coronary sclerosis, syphilitic aortitis, or cardiac infarct. Lian (1931) has described similar cases and concluded that a " thoraco-brachial neuralgia " resulted from the repeated shocks to the brachial plexus by the anginal paroxysms. He mentioned the similarity to arthritis of the shoulder. Edeiken and Wolferth (1936) reported 14 cases with persistent pain in the shoulder following myocardial infarction, and Boas and Levy (1937) described 21 cases. In 29 of these 40 cases the left shoulder was involved, but some patients with radiation of the anginal pain to the right shoulder subsequently developed chronic right shoulder disability.

TABLE II

CHRONIC SHOULDER PAIN PRECEDING ANGINA PECTORIS OR CARDIAC INFARCTION

Case No.	Age	Site and Duration of Shoulder Pain before Cardiac Symptoms appeared *	Subsequent Course of Shoulder Pain	Anginal Attacks (A.P.) and Coronary Thrombosis (C.T.)	Remarks
13	50	L. .. .. 2 yr.	Not known	Post. C.T.	Incapacitated by shoulder pain
14	59	R. .. .. 4 yr.	Present 1 yr. later	A.P.	Inability to use arm
15	46	L. .. .. 1 yr.	Present 3 yr. later	A.P.	Incapacitated by shoulder pain
16	48	L. .. .. 1 yr.	Improved	A.P.	Paroxysmal nocturnal dyspnœa
17	55	R. .. .. 3 yr.	Died suddenly 9 mo. later	A.P.	Consulted neurologist
18	83	R. .. .. †	Not known	A.P.	Osteoporosis in both shoulders
19	45	R. .. .. 3 yr.	Worse 9 mo. later	A.P. Ant. C.T.	Right subacromial bursitis
20	59	L. .. .. 7 yr.	Not known	A.P.	Incapacitated by shoulder pain
21	45	R. .. .. 5 mo.	Improved 3 mo. later	A.P. C.T.	Very severe before infarction
22	43	L. .. .. 5 yr.	Improved	A.P. Ant. C.T.	Infarction commenced with left shoulder pain

* L. and R. indicate shoulder affected.   † Simultaneous onset 1 year before.

In the present series are 25 patients with angina pectoris and/or myocardial infarction, in whom chronic shoulder and arm pain formed a prominent complaint. In 10 the shoulder complaint preceded the angina or infarction by months or years (Table II). In 15 it followed and was the outstanding feature during convalescence (Table III).

TABLE III

CHRONIC SHOULDER PAIN FOLLOWING ANGINA PECTORIS OR CARDIAC INFARCTION

Case No.	Age	Shoulder affected and Duration of Angina when Shoulder Pain appeared *	Duration of Shoulder Pain	Anginal Attacks	Electrocardio-gram
23	59	R. .. 0	3 years	Mild	—
24	54	L. & R. 2 years	1 year	Severe †	Inv. T_1 & T_2
25	53	L. .. 2 weeks	2 weeks	Severe	Slurred QRS waves. Inv. T_3
26	64	L. .. 10 months	14 months	Severe	T_1 & T_2 diphasic. Inv. T_3
27	48	L. .. 1 week	3 weeks	Severe.	—
28	52	L. & R. 2 months	10 months	Moderate †	T_3 diphasic, later inverted
29	52	L. & R. 2 months	6 months	Severe	T_1 & T_4 flat
30	67	R. .. 1 week	1 year	Moderate	Flat T_4
31	59	L. .. 2 months	6 months	Moderate	—
32	49	L. & R. 1 month	5 months	Severe	T_1, T_2, T_3 low
33	59	L. & R. 18 months	6 months	Moderate †	—
34	52	L. .. 19 months	5 months	Mild	Normal
35	66	L. .. 5 years	1 week	Mild	Normal
36	65	L. .. 0	18 months	Moderate †	Late inv. T_1. High T_3
37	47	L. .. 30 months	6 months	Severe	Low T_2

* L. and R. indicate the shoulder affected.
† A diagnosis of myocardial infarction was made in these cases.

Case 13. *Chronic pain in left shoulder for 2 years before cardiac infarction*

Male, aged 50. Dyspepsia for 15 years. Dyspnœa on exertion and pain, not related to exertion and lasting several hours, twice a week, in left shoulder and arm, for past 2 years. No chest discomfort. Some general weakness and pallor for 6 months. Chronic shoulder pain had increased in severity lately, preventing sleep. Forced to give up work because of it 6 months ago. Weight loss of 15 lb. during past year. Two weeks ago pain became much worse and he entered hospital. Dyspnœic. B.P. 150/85. EC. showed inverted T_2 and T_3, and prominent Q_3. Gradual improvement while under observation.

Case 22. *Recurrent persistent pain in left shoulder for 5 years before cardiac infarction*

Male, aged 43. Well and active till 5 years ago. Then pain in left shoulder and down the arm to fingers, persisting, on and off, for 2 years ; artificial heat and light prescribed without improvement. A few months ago at night, a severe grinding pain in the left elbow and forearm spreading upwards to the shoulder, and lasting an hour. Next day the left arm pain was worse and he felt exceedingly ill, with slight fever, and was in bed for several weeks. Now complains of typical angina, spreading to left arm. B.P. 150/90. EC. showed lead III inverted.

Case 24. Persistent pain in both shoulders for 1 year ; angina for 3 years

Male, aged 54. Angina pectoris 3 years. No radiation. Attacks becoming more frequent, till three times a day ; incapacitated for 2 years. One year persistent pains in both shoulders, especially left, radiating down both arms in anginal attacks. Two severe attacks 6 weeks ago in which pain was persistent and unaffected by nitrites ; " terrific " pain in left shoulder during one attack, since when pain in left shoulder and arm almost constant. Aortic regurgitation. B.P. 230/60. Heart enlarged to left. EC., inverted T_1 and T_2.

Case 25. Persistent left shoulder pain 2 weeks after onset of angina

Male, aged 53. Anginal attacks for one month with radiation to left arm. Three severe attacks in all before onset of constant pain in left shoulder ; this had been present 2 weeks when examined. Some dyspnœa on exertion. B.P. 155/80. Moderate enlargement of heart. Aorta slightly tortuous. EC., T_3 inverted. X-ray of left shoulder, no abnormality. Pronounced atrophy of left shoulder-girdle muscles, with moderate limitation of all voluntary but not of passive movements. No tenderness or fullness in region of subacromial bursa.

DISCUSSION

In this group we have described an affection of the shoulder and, arm in patients with angina, characterized by constant dull pain, limitation of movement, and weakness or lameness of the arm. The pain is not usually provoked by exercise, but may be aggravated by use of the affected arm, as for carrying. Examination of the shoulder reveals no local lesion. Calcification in the subdeltoid bursa or of the supraspinatus tendon is rarely encountered. The pain is intractable, not unlike a causalgia, and may shift from one shoulder to the other. Usually, in angina with left-sided radiation, it affects the left shoulder and arm ; with right-sided radiation, the right shoulder and arm. This is by no means constant, however, and in this sense there was agreement in 6 cases and disagreement in 2, the remainder showing no radiation. Tenderness over the shoulder is infrequent, but atrophy of the shoulder girdle muscles has been seen. In Case 25 pronounced atrophy of the muscles of the left shoulder girdle developed four weeks after a myocardial infarction. Active abduction and external rotation were limited but passive movements were normal. No tenderness, crepitus, or pain on manipulation were discovered ; X-ray showed no abnormality. Many patients complain that the pain is much worse at night and prevents sleep.

The disability may precede or follow angina pectoris or cardiac infarction ; if present before infarction occurred it is usually intensified. The shoulder pain may also be the outstanding feature of the coronary occlusion, overshadowing the substernal pain. In those instances where shoulder pain preceded the appearance of other symptoms, relief was frequently sought of the neurologist, orthopædist, or physiotherapeutist. Sedatives, massage, and heat are usually without much success, and morphia is often needed in the acute phase. The administration of nitrites has no effect upon the constant aching, unlike the success frequently encountered in the eccentric paroxysmal pain of the first group. It thus seems that vascular spasm plays no part in

its production. The affection appears to run its course despite treatment and subsides spontaneously.

The mechanism of this shoulder and arm pain is obscure. There is rarely any local lesion to account for it. A few authors, however, have described the intensification of the symptoms of subacromial bursitis following a myocardial infarction (Libman, 1935 and Boas and Levy, 1937), and one such case is to be found in our series (Case 19). It is doubtful if this is the explanation for all such cases of shoulder pain. In the absence of localized tenderness or fullness beneath the deltoid or calcification within the sac, it would be difficult to make a diagnosis of bursitis. Libman thinks that one frequently finds spondylitis, bursitis, intercostal neuralgia, and other " gouty " disorders associated with true angina pectoris, because they have the same origin.

But in our patients there was no evidence of a previous bursitis, and even during the height of the disability no indication of a local lesion. The pain was not always felt in the shoulder region, but sometimes in the muscles of the arm or forearm when movements at the shoulder were entirely free. At times the pain was replaced by a " deadness " or " heaviness " or " lameness." The hand of the affected arm was sometimes cold and numb ; cyanosis, pallor, or œdema of the arm were not observed. Similar transient symptoms and signs are well-known sequels to attacks of angina pectoris. In our patients these symptoms are intensified and prolonged ; they are the main complaint, differing only in degree and duration from the transient post-anginal phenomena. A localized lesion in the shoulder has not been invoked to explain the latter and is probably unnecessary in the former.

Much of the discussion on the extra-cardiac site and radiation of cardiac pain dates from the observation by Mackenzie (1923) that in one of his patients with an abscessed tooth the anginal pain radiated to that tooth ; yet irrefutable instances are rarely, if ever, encountered in actual practice. Even if a local lesion is demonstrated in the path of an eccentrically radiating anginal pain, the obvious conclusion is highly dangerous, as twice as many instances of similar radiation can be cited in which no obvious local lesion existed. Such was the condition in Case 2, where the facial localization of the pain led to a suspicion of trigeminal neuralgia.

In view of the hypotheses put forward to account for the bizarre radiation of some anginal pains and in view of the popularity of the concept of " sensitization of pathways," it is instructive to consider the following history. A man, aged 60, had sustained a compound fracture of the *right* arm 14 years previously, necessitating amputation below the shoulder. The pain in the stump became constant and intolerable, so that on several occasions novocain injection was performed. In the absence of any relief, and because of the severity of the pain, numerous surgical procedures were attempted during the following 7 years—section of roots of the brachial plexus, repeated novocain blocks, laminectomy with section of roots, and alcoholic injection of the stellate ganglion—but the pain still continued, when anginal attacks made their appearance. The pain radiated to the *left* arm, and was relieved by nitrites. A more persistent pain in the left arm was unrelieved by nitrites and unaffected by

exercise. Novocain injection of the left stellate ganglion afforded much relief. The patient died suddenly of myocardial infarction. Such an example lends little credence to the theory of " sensitization of pathways " in the determination of the radiation of anginal pain. The *right* brachial plexus had been subjected to repeated surgical procedures and causalgic pains were intractable for 14 years, yet subsequent anginal pains radiated to the *left* arm.

To return to our main thesis. What, then, is the nature of persistent shoulder and arm pain in coronary arterial disease ? In some there may be a local lesion of muscle or bursa aggravated by the cardiac nerve irritability, but in others there may be simply an irritation of the cardiac sympathetic plexus in the presence of myocardial ischæmia. In favour of the former theory, shoulder pain is extremely common whether there is angina pectoris or not, but such an explanation seems unlikely for every case. The pain is referred to the shoulder and arm, usually of the left side, and is associated with the attacks of angina pectoris. The constant nature of the pain could be accounted for on the basis of the theory of " summation." Intermittent showers of impulses, travelling over pain fibres, may induce constant pain through summation at synapses ; the central neurones, then, most probably discharge continually and give rise to constant pain.

CONCLUSIONS

Disease of the coronary arteries may manifest itself by paroxysmal, extra-thoracic pain on effort. Twelve cases are described in which bouts of pain in one or both arms were, for varying periods of time, the only manifestation of ill health. Such pains, constricting in character, appear suddenly on exertion ; they are felt usually at the wrists, forearms, or elbows, and are relieved by rest or by nitroglycerine. Fatal attacks may ensue, attacks in which the pain remains located in the arm. In others typical anginal paroxysms or cardiac infarction subsequently develop.

Classical angina pectoris or cardiac infarction is frequently complicated by persistent pain in the shoulder and upper arm. This pain is of a dull, aching character, diffusely felt, usually on the left side in left-sided and on the right side in right-sided anginal attacks. The pain bears no direct relation to exercise and is not relieved by nitroglycerine. It may precede or follow angina pectoris or cardiac infarction by weeks or even by years. Ten cases are described in which chronic shoulder and arm pain was followed, 5 months to 5 years later, by typical angina pectoris. This pain may be incapacitatingly severe during accesses of coronary insufficiency and may then be the outstanding therapeutic problem. Fifteen cases of similar pain following angina pectoris or cardiac infarction are recorded.

The mechanism of the chronic pain is obscure. A local lesion of the shoulder or arm can rarely be demonstrated, though exacerbation of a pre-existing sub-acromial bursitis may be the explanation in some cases. Often the pain may be interpreted as one of the varied referred phenomena encountered in the arms in angina pectoris and cardiac infarction.

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THE ACTION OF DIGITALIS IN HEART FAILURE WITH NORMAL RHYTHM

BY

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While it is generally accepted that digitalis may be of benefit in cases of congestive heart failure with normal rhythm, there is disagreement as to the frequency of such benefit, as to whether the ætiological type of heart disease influences the response, and as to the mechanism whereby the improvement is brought about. The present work deals in some measure with these three points.

It is not proposed to make an exhaustive survey of the earlier work, for this has been handled recently by Gavey and Parkinson (1939). They concluded that demonstrable benefit occurred in about half of the cases and that those with rheumatic heart disease responded better than all other ætiological types. They went further : they stated that cases of rheumatic heart disease responded better than other types, whether there was normal rhythm or auricular fibrillation, and since it is the rheumatic cases that characteristically fail with fibrillation they made the interesting suggestion that this might explain the time-honoured notion that heart failure with fibrillation responds better to digitalis than heart failure with normal rhythm. With regard to the third point : while in the common view digitalis improves the functional efficiency of the failing heart by direct action upon it, there are other opinions. Slowing of the heart rate with lengthening of the diastolic rest period is usually associated with the improvement and has been held responsible for it. There is also the view of Dock and Tainter (1930), supported by Katz and his co-workers (1938), that digitalis produces its beneficial effect upon failure with normal rhythm by its constrictor action upon the hepatic vessels, particularly the hepatic vein sphincter, operating " as a bloodless venesection." This conclusion is based on experiments with anæsthetized dogs without organic heart disease and has not been confirmed in man with congestive heart failure.

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METHODS OF INVESTIGATION

In accordance with the back pressure theory, the essential effect of right ventricular failure is elevation of the systemic venous blood pressure. The

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degree of right ventricular failure was therefore estimated by direct measurement of the pressure in the antecubital vein, a procedure which is both simple and accurate. Other criteria were not used as a measure of the degree of congestive heart failure, and this needs no apology, for symptoms cannot as yet be measured accurately ; the size of the liver is difficult to assess clinically owing to alterations in the height of the diaphragm and to difficulty in determining its upper border ; œdema is capricious ; accurate measurement of diuresis requires control of too many factors ; and direct measurement of the cardiac output is complicated and often inaccurate, except in most experienced hands, and is not a measure of congestion. It may be said, however, that in no case was a fall in venous pressure accompanied by aggravation of symptoms, apparent enlargement of the liver, increase of œdema, or by apparent diminution of urinary output. The reverse was usually true and obvious diuresis occurred in some cases.

The venous blood pressure was determined in the following way. The patient was inclined at an angle of 45 degrees from the hips upwards, and the right shoulder and arm were bared and the arm placed comfortably on pillows well away from the trunk and approximately at the level of the fourth sterno-chondral junction. A wide-bore needle attached to a rubber tube was inserted into the right antecubital vein and strapped in position, the rubber tube being connected to an upright graduated glass tube fitted at its bottom with a T-piece, to which was connected a citrate reservoir, the whole system being filled with 3·8 per cent sodium citrate (see Fig. 1). The apparatus was supported by a
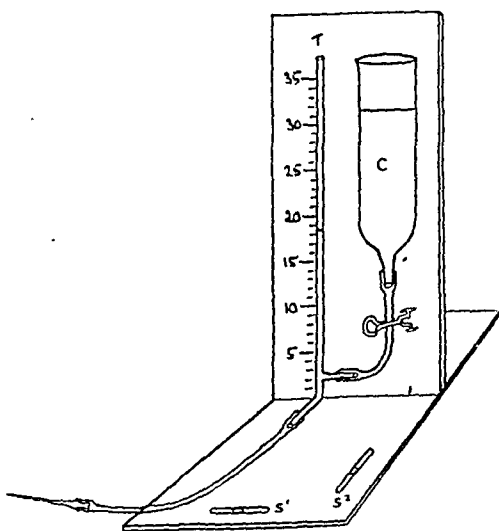
FIG. 1.—Apparatus for continuous measurement of the venous blood pressure.
T. Graduated glass tube.
C. Reservoir of 3·8 per cent sodium citrate.
S¹ and S² spirit levels.

wooden frame fitted with spirit levels so that the bottom of the graduated tube could be set at the level of the fourth right sterno-chondral junction by suitable manipulation of the base of the frame, and by releasing the cock momentarily

every two or three minutes in order to flush the needle with citrate, continuous venous pressure measurements could be made indefinitely. (For normal controls·see Wood, 1937.)

Although this work is primarily concerned with right ventricular failure, i.e. heart failure with systemic congestion, a few cases of isolated left ventricular failure were also studied, and in these the arm to tongue circulation time, as estimated by the decholin method (Wood, 1937), was used as the most simple and accurate measure of the degree of pulmonary congestion.

To ensure proper control, all cases of heart failure with normal rhythm admitted to hospital were put on absolute rest and received no treatment other than sedatives for a period not less· than a week and averaging a fortnight ; patients who showed significant improvement were excluded from further study. The others then received digitalis in doses of 9 grains the first day, 6 grains the second day, and 3 grains of the powdered leaf thereafter, until therapeutic effects or symptoms of intoxication were observed.

By such means it was possible to determine the frequency of the benefit derived from digitalis, and whether certain ætiological types of heart disease responded better than others, but the method was too crude to provide any information as to the mechanism of digitalis action. For this purpose special observations were made. The subjects were kept at complete rest and the venous blood pressure recorded continuously ; after a period of at least half an hour, when a steady level had been reached, 1·5 mg. of digoxin was injected intravenously. The effects were then studied in relation to the pulse rate and to the size of the liver and spleen, and will be described in more detail later.

RESULTS

Frequency of Benefit

There were fifteen cases with right ventricular failure and normal rhythm, fourteen of which received demonstrable benefit from digitalis.· Serial venous pressure measurements showed that the improvement was abrupt, and this is
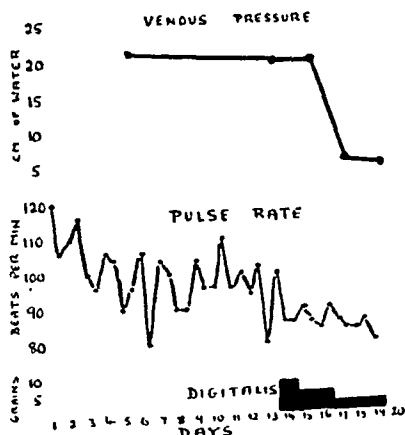
FIG. 2.—The action of digitalis on the venous blood pressure and pulse rate in a case of hypertension with right ventricular failure and normal rhythm.

illustrated in Fig. 2, which is typical of the series. Table I shows the venous blood pressures and the average pulse rates before and after digitalis therapy in each of the fifteen cases, and it will be seen that with one exception the drop

TABLE I·

THE VENOUS BLOOD PRESSURE AND PULSE RATE BEFORE AND AFTER DIGITALIS IN RIGHT VENTRICULAR FAILURE WITH NORMAL RHYTHM

Case	Ætiological Diagnosis	Venous Pressure			Pulse Rate			Effect
		Before	After	Fall	Before	After	Fall	
1	Hypertension	22·5	5·0	17·5	95	85	10	Good
2	Hypertension	20·0	5·0	15·0	100	90	10	Good
3	Hypertension	20·0	10·0	10·0	100	95	5	Good
4	Rheumatic mitral stenosis	18·0	5·0	13·0	95	75	20	Good
5	Doubtful	17·5	7·5	10·0	80	80	0	Good
6	Doubtful	c. 20	<10	>10	105	75	30	Good
7	Cor pulmonale	>20	Normal	>10	90	80	10	Good
8	Hypertensive	22·5	20·5	—	95	85	10	None
9	Doubtful	c. 20	Normal	>10	110	90	20	Good
10	Hypertension	21·0	Normal	>10	100	85	15	Good
11	Hypertension	15·0	6·0	9·0	108	84	24	Good
12	Old hypertension	21·0	12·0	9·0	108	104	4	Good
13	Cor pulmonale	17·0	9·0	8·0	105	90	15	Good
14	Hypertension	15·0	5·0	10·0	Chart lost			Good
15	Cor pulmonale	16·5	8·0	8·5	112	112	0	Good

in the venous pressure was always considerable. Two of the three in which the ætiological diagnosis was not established came to autopsy later, and though the nature of the heart disease even then remained obscure, there was nothing to suggest that they were rheumatic. The third case likewise showed no clinical evidence of rheumatism. The patient who received no benefit died suddenly in rather a curious way. He had massive œdema and weighed twenty stone, and after the failure of digitalis therapy, 2 c.c. of salyrgan injected intravenously resulted in an enormous diuresis, followed by slowing of the pulse rate from ninety to fifty beats per minute and sudden death. During the final two days his weight dropped 22 lb.

There were five cases with isolated left ventricular failure, congestion being confined to the pulmonary circuit. Serial observations on the arm to tongue circulation time showed significant improvement in four, but not in the fifth, which proved at autopsy to be one of periarteritis nodosa. Table II shows the arm to tongue circulation times and the average pulses rates before and after digitalis therapy in these five cases of left ventricular failure with normal rhythm. Fig. 3 illustrates the changes in the four cases with demonstrable improvement.

Thus, out of a series of twenty cases of congestive heart failure with normal rhythm, fifteen right and five left, eighteen responded to digitalis and two did not. Though the series is small it was well controlled and improvement was accurately measured and not a matter of opinion.

TABLE II

THE CIRCULATION TIME AND PULSE RATE BEFORE AND AFTER DIGITALIS IN LEFT
VENTRICULAR FAILURE WITH NORMAL RHYTHM

Case	Diagnosis	Circulation Time (sec.)			Pulse Rate			Effect
		Before	After	Fall	Before	After	Fall	
16	Hypertension (Periarteritis)	30	29	—	90	90	0	None
17	Hypertension	36	21	15	95	95	0	Good
18	Ischæmic	25	18	7	90	80	10	Good
19	Hypertension	40	22	18	110	95	15	Good
20	Hypertension	27	22	5	75	60	15	Fair
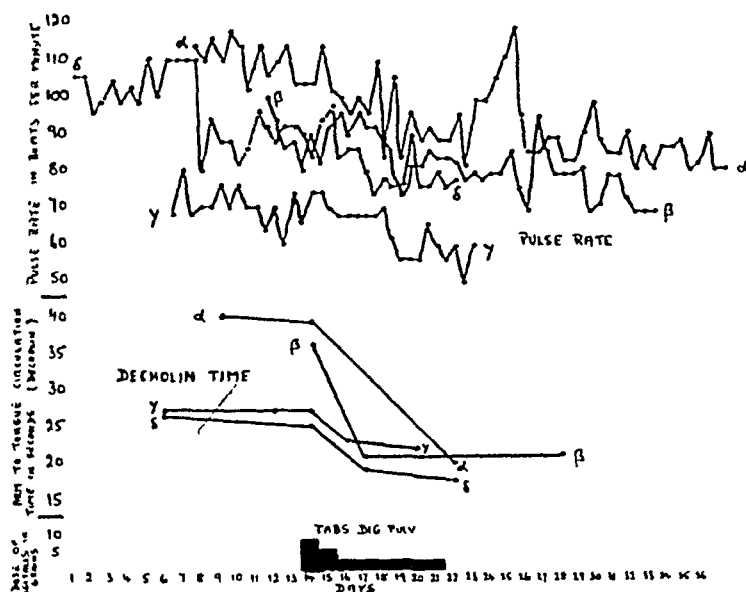
FIG. 3.—The action of digitalis on the arm-to-tongue circulation time and on the pulse rate in four cases of isolated left ventricular failure with normal rhythm.

The letters show which pulse chart corresponds to each circulation time chart. The length of the block representing digitalis therapy corresponds to case *γ*, the drug being used for a longer period in the others.

Influence of the Ætiological Type of Heart Disease

The ætiological diagnosis has been given in Tables I and II. There were twelve cases with hypertensive heart disease, three with chronic cor pulmonale, one with mitral stenosis, one with ischæmic heart disease, and in three the diagnosis of the condition was obscure (see p. 135). Thus, although eighteen out of twenty responded to digitalis, only one of these was rheumatic. It follows that if rheumatic heart disease responds better to digitalis than all ætiological types, it must respond very well indeed, for eighteen out of twenty is a proportion not often exceeded.

Mechanism of Digitalis Action

1. *Influence of the pulse rate.*—In all but three of the long period studies the pulse rate fell with digitalis, on the average from 98 to 85 beats per minute. In two of the three with no fall in pulse rate digitalis effected an improvement. It has already been stated that two cases did not respond to digitalis. One of these showed a fall in pulse rate (from 95 to 85) and the other did not. Thus, with this crude method, it appears that although a fall in pulse rate is usually associated with improvement from digitalis therapy, it is not essential. (See Tables I and II.)

This point was investigated more thoroughly by means of four special observations. In the first (Fig. 4), 1 mg. of digoxin was injected intravenously
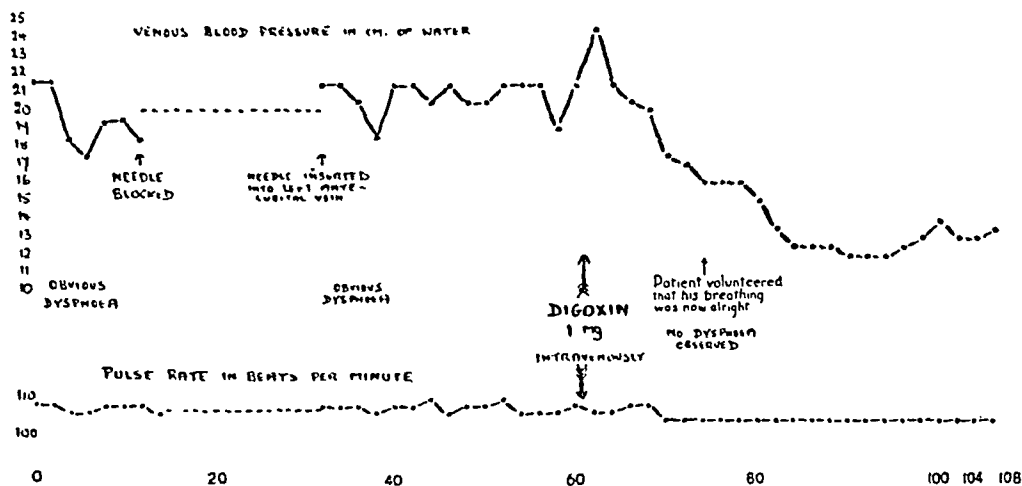
FIG. 4.—Continuous readings of the venous blood pressure and pulse rate in a case of right ventricular failure treated with intravenous digoxin.

when the venous blood pressure level had been steady at 21 cm. of water for half an hour, and the pulse rate consistently between 105 and 110 beats per minute for an hour. The figure shows the rapid fall of the venous pressure to 12 cm. of water, and the very slight drop in pulse rate to 104 beats per minute. This observation was repeated in another patient, and whereas the venous blood pressure fell from a steady level of 15 to 8 cm. of water, the pulse rate remained constant at 112 beats per minute throughout. In the third observation a larger dose of digoxin (1·5 mg.) was used, and as the venous blood pressure fell the pulse rate dropped sharply from 105 to 90 beats per minute (Fig. 5) ; atropine (1 mg.) was then injected intravenously and the pulse rate climbed back quickly to 105, but the venous pressure continued to fall and finally reached normal limits. In the fourth observation chance proved an ally. After 1·5 mg. of digoxin the venous pressure fell from 15 to 7 cm. of water, while the pulse rate rose steadily (Fig. 6). After a time the patient admitted that she had been suppressing a strong desire to micturate, but could hold her water no longer, and as it was not expedient for her to move, a catheter was passed and during its manipulation the venous pressure rose abruptly on account of her respiratory reactions. As the urine flowed the pulse rate
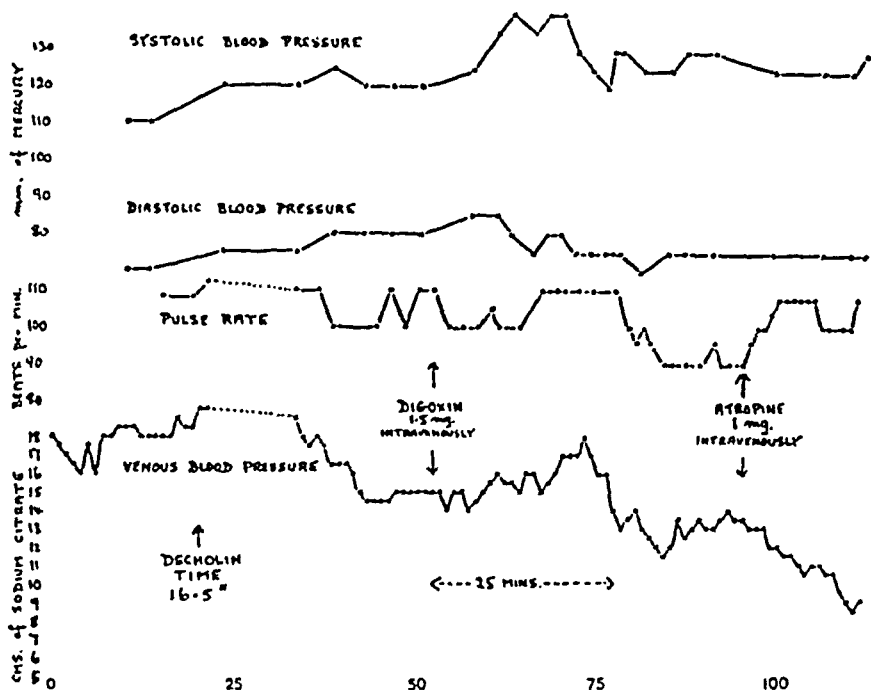
FIG. 5.—Continuous readings of the venous blood pressure and pulse rate in a case of right ventricular failure with normal rhythm treated with intravenous digoxin; the pulse rate fell as the venous pressure dropped, but after atropine it rose again to its previous level while the venous pressure continued to fall. (Note the slight rise of systolic blood pressure.)
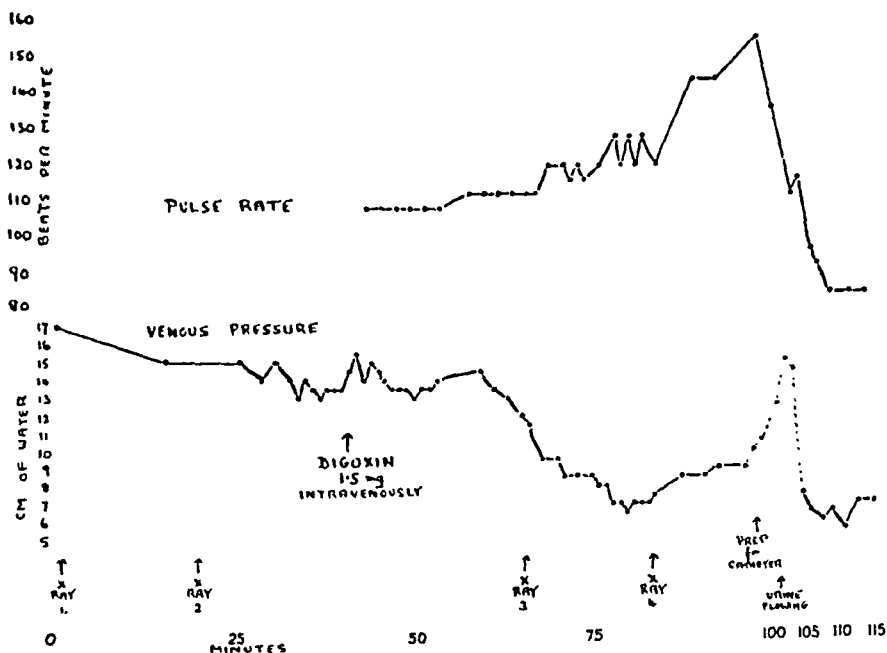
FIG. 6.—Showing how the pulse rate rose while the venous pressure fell after digoxin in a case of hypertension with right ventricular failure and normal rhythm; the curious behaviour of the pulse rate was due to a suppressed desire to micturate.

Serial X-ray films of the liver and spleen made radio-opaque by thorotrast were obtained in this case. The times at which these films were taken are marked.

dropped sharply from 156 to 84 beats per minute and the venous pressure fell again to normal.

It is clear from these four observations that the drop in venous blood pressure effected by digitalis therapy in cases of congestive heart failure with normal rhythm is dissociated from coincident changes of pulse rate.

2. *Influence of hepatic venous constriction.*—If the theory of Dock and Tainter (1930), so ardently supported by Katz (1938), that digitalis acts like a " bloodless venesection," by constricting the hepatic veins and damming up the blood in the liver and spleen, be correct, then the liver and spleen should enlarge, as indeed these authors have demonstrated in animals. Clinically it is difficult to be sure of the upper borders of these viscera, but with the aid of thorotrast they may be visualized by means of X-rays. A patient with·congestive heart failure and normal rhythm, with a bad prognosis, was injected with 75 c.c. of thorotrast intravenously in three divided doses at intervals of two days, until at the end of the week the liver and spleen were well seen on X-ray films. A special observation with 1·5 mg. of digoxin, similar to those already described, was then performed on a horizontal X-ray stand, so that control and serial X-ray films of the liver and spleen could be taken without disturbing the position of the patient. As the inferior border of the liver was exceptionally easy to feel, its position was frequently checked clinically by making serial marks on the abdominal wall. The venous blood pressure behaved as usual and fell from 14 to 7 cm. of water (Fig. 6). Tracings from
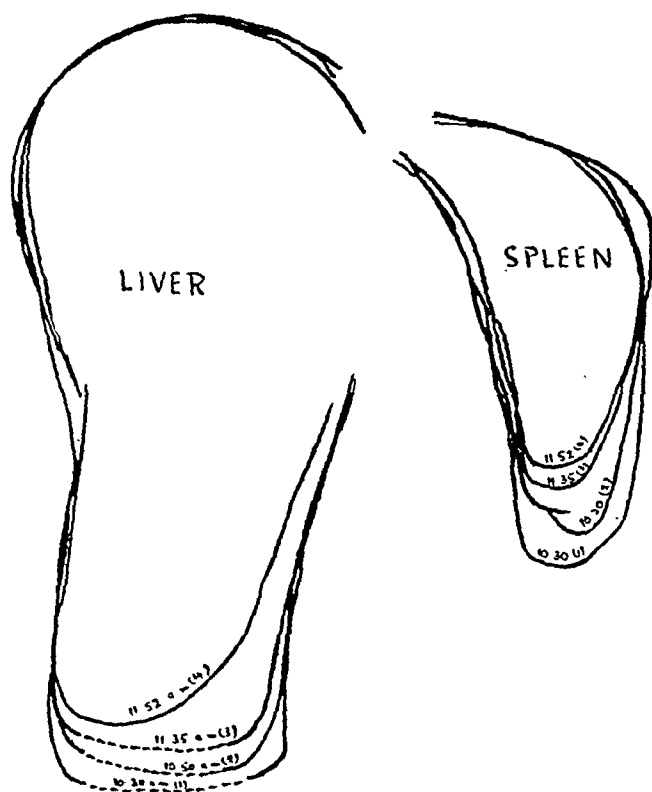
FIG. 7.—Superimposed tracings of the X-ray films of the liver and spleen from the case illustrated in Fig. 6. The reduction in size of the liver was checked clinically.

the serial X-ray films have been superimposed in Fig. 7, and it will be seen that coincident with the fall in venous pressure there was considerable reduction in size of both liver and spleen. This was supported by clinical evidence in respect of the lower margin of the liver, which was observed to move upwards more than an inch. It follows that the fall in venous pressure was not due to hepatic venous constriction or to portal venous constriction above the mouth of the splenic vein.

CONCLUSIONS

1. Digitalis effected demonstrable improvement in eighteen out of twenty cases of congestive heart failure with normal rhythm. This was judged by serial measurements of the venous blood pressure in those with systemic congestion, and of the arm-to-tongue circulation time in those with pulmonary congestion.

2. Since it has been stated that rheumatic heart disease responds better to digitalis than other ætiological types, it is of interest that only one of the present series was rheumatic.

3. Observations showed that the fall in venous blood pressure following intravenous digoxin was not due to slowing of the heart.

4. A single observation refuted the view that the beneficial action of digitalis is due to its constricting effect upon the hepatic vein.

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PERIPHERAL CIRCULATION BY PHOTO-ELECTRIC RECORDING

.BY

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There is a growing tendency in modern medicine to rely on accessory methods and tests for clinical information, though nothing can really take the place of accurate observation and experience. It is the purpose of this paper to add yet another investigation to clinical science, but it is done to further the understanding of certain cardiovascular conditions and not to supplant the present methods of examination.

Numerous methods have been employed in the study of the peripheral circulation. In animal experiments the stromuhr is a familiar instrument, and by this means much interesting information has been obtained and many fundamental physiological facts have been established.

A more recent method of Rein (1928) involves the installation of a thermo-electric couple unit on the vessel wall. It consists of a pair of copper-constantin junctions between which is a heating element—the proximal at blood temperature and the distal at a higher temperature because of the warming effect of the heating element. This difference in temperature creates an electrical potential, which is recorded on a galvanometer, and the faster the blood flows past the point of heat application, the less heat it will acquire and the shorter will be the excursion of the galvanometer. Thus, after calibration, the deflection of the galvanometer will be a measure of the rate of blood flow. This method was improved upon by Herrick, Essex, Baldes, and Mann (1936), so that it is now applicable even to the coronary circulation.

Plethysmography has added much to the physiology of the circulation. In principle it depends upon the alteration of volume with changes in its blood content. Much apparatus has been devised for purposes of recording, at first of a simple type such as the Marey tambour or piston recorder, and later more refined optical and photographic methods. Goetz (1939) and Matthes (1935) transmitted the volumetric fluctuations to a graduated pipette or capillary tube, while Baldes and Corbeille (1928–9) and Bolton, Carmichael, and Stürup (1936) converted the volume changes to pressure changes by means of a water or membrane manometer. Sir Thomas Lewis has employed plethysmography to

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its best advantage, and to him we owe much of our knowledge concerning the physiology and pathology of the peripheral circulation. However, this method involves many technical difficulties, and the apparatus is bulky and inconvenient for routine or emergency investigation in the clinical wards. There is also a great deal of controversy over the interpretation of the results (Goetz, 1939), owing to possible errors inherent in the instrument itself and lack of detail in the records obtained.

METHOD OF INVESTIGATION

A more direct approach to the study of the peripheral circulation may be made by transillumination of the vascular bed, either by directly transmitted light or by reflected light that has penetrated the skin's surface. The intensity of the emergent beam will be found to fluctuate, paralleling in time and quantity the ebb and flow of blood circulating through the transilluminated tissue. These rhythmical changes are converted into electrical energy by a photo-electric cell. In turn, a capacity-coupled amplifier transforms the current so produced into potential energy which is recorded on an ordinary electrocardiograph.

Fig. 1 shows the actual apparatus, consisting of a standard model electro-
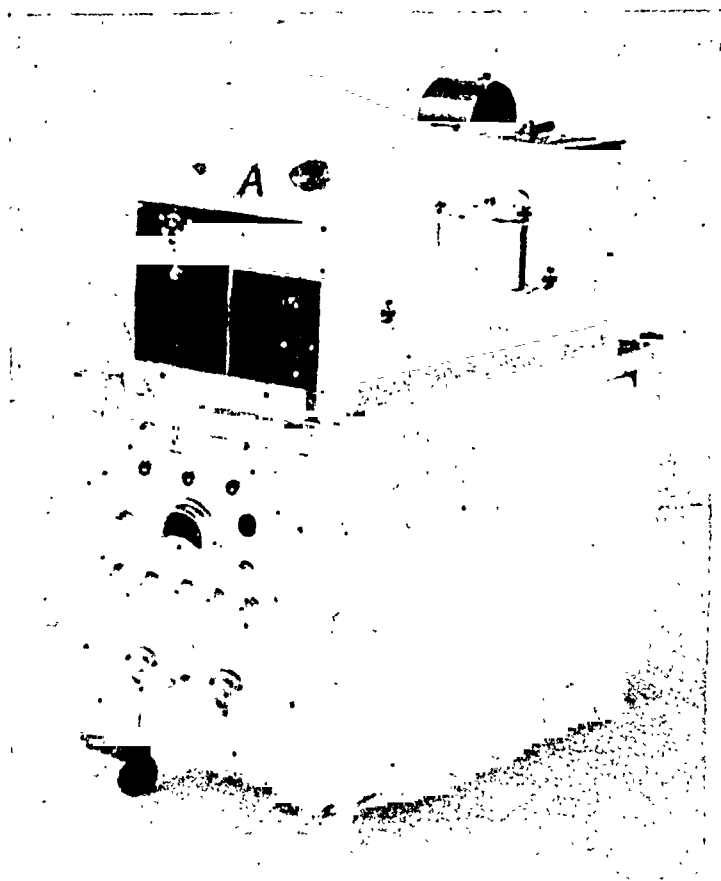
FIG. 1.—Combined electrocardiograph and tissue circulation recorder. A is shown in more detail in Fig. 3, and the amplifier panel board (here shown in front is given in more detail in Fig. 6.

cardiograph, amplifier, and battery, all mounted on a portable oak frame. It was found best to power the entire apparatus by a 12-volt battery, as this eliminated the need for long leads, avoided the possibility of a fluctuating and irregular mains supply, and enabled the entire apparatus to be shielded against electrical interference.

The unit for transillumination of the fingers or toes is shown in Fig. 2. The source of light is a focusing lamp with two thirds of the sphere silvered to provide a reflecting surface. The light is thus concentrated on the tissues and provides a maximum of light with a minimum of heat.
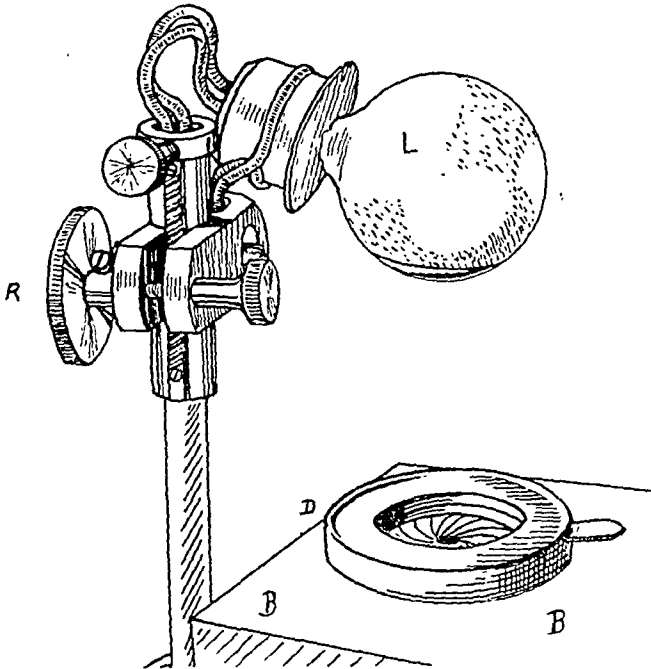
FIG. 2.—The photo-electric cell unit.

L, lamp ; R, ratchet device ; D, iris diaphragm; and B, metal box housing the photo-electric cell.

The aperture in the iris diaphragm controls the amount of light that is allowed to fall on the photo-electric cell mounted beneath. The object to be transilluminated is placed over the aperture and the distance of the light source is regulated by the ratchet mounting device. The intensity of the light is adjusted by a variable resistance which is mounted in the electrocardiograph chassis (Fig. 3).

The Photo-electric Cell.—This is of the photo-emissive selenium type, No. PE 7B (B.T.H.). It is mounted by means of a four-pin holder on a wooden block, which in turn is fastened securely to the lid of the metal box. The inside of the container is painted black to minimize the possibility of extraneous light falling on the sensitive cell. The shielded lead from the cell, together with the flex lead to the lamp, is encased in rubber tubing to be conducted to the instrument proper.

It is of the utmost importance to realize that any abnormalities in this part
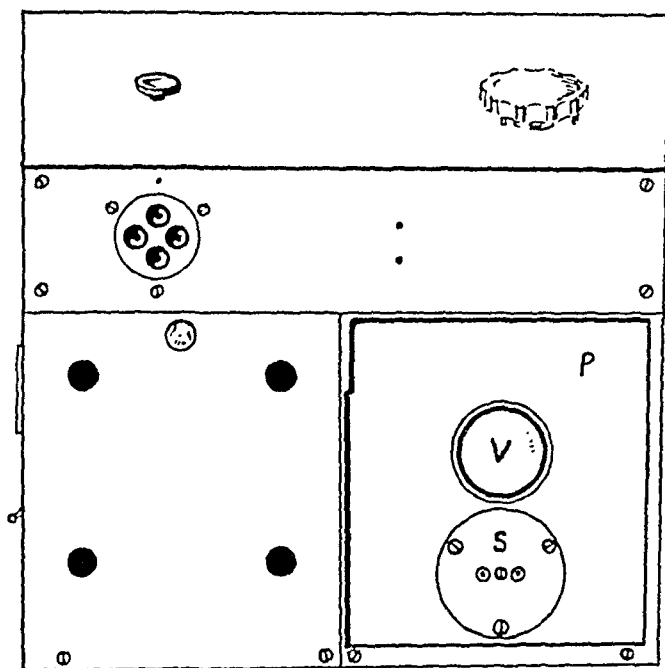
FIG. 3.—Panel mounting in electrocardiograph chassis.
P, panel ; V, variable resistance control ; and S, lamp socket.

of the apparatus will be amplified several thousand times and result in extreme distortion of the subsequent records. Thus all precautions must be taken towards adequate insulation and shielding.

The Amplifier.—The actual circuit of the amplifier is presented in Fig. 4 (on the opposite page). Its components are standard materials and its construction involves no technical difficulties. However, the values throughout the circuit are very essential and must be strictly adhered to. While an amplifier cannot create new wave forms, it can distort those already present.

A few of the different complexes obtainable simply by varying the values in the amplifier circuit are shown in Fig. 5, and this emphasizes the need for maintaining the exact standards suggested. Previous methods employed by Hertzmann (1937) and by Matthes and Hauss (1938) further illustrate this point. It was thus necessary to search for a means of testing the accuracy of the wave-forms as they were translated by the amplifier. Since the rate, rhythm, and amplitude of an electrocardiogram coincides to a great extent with the wave forms of tissue circulation, it was decided to make this the criterion of accuracy of the amplifier unit. The method used was as follows : A normal electrocardiogram is taken. The amplifier is then introduced into the circuit and the string is accordingly tightened to compensate for the increased swing of the galvanometer. The artifact due to the momentum of the galvanometer string when swinging in a wide amplitude was thus avoided. The values in both the input and output circuits of the amplifier were then altered in the direction minimizing distortion. The circuit described here gives an almost identical image of the original cardiogram.
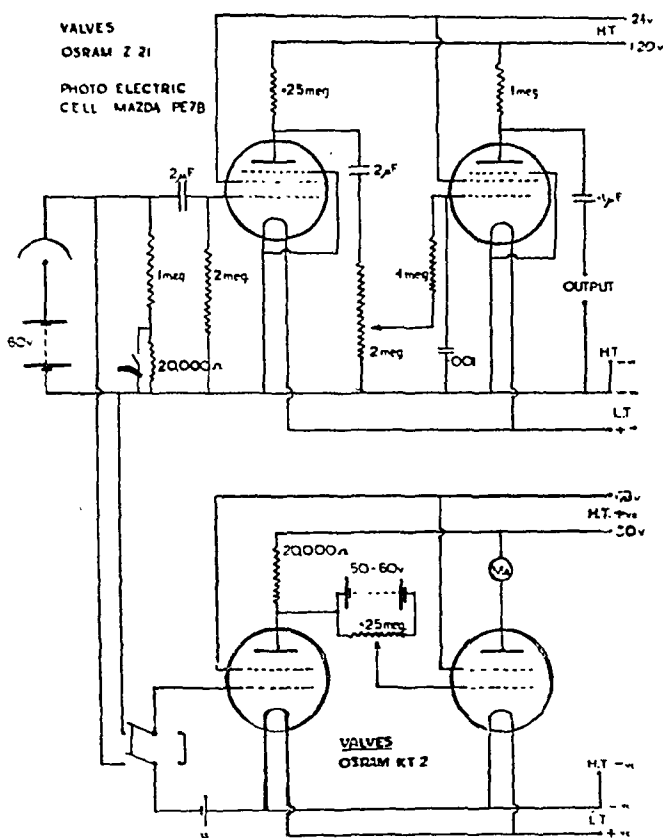
FIG. 4.—The combined electrical circuit of amplifier (above) and photometer (below). The values throughout the circuit are very essential and must be adhered to strictly.
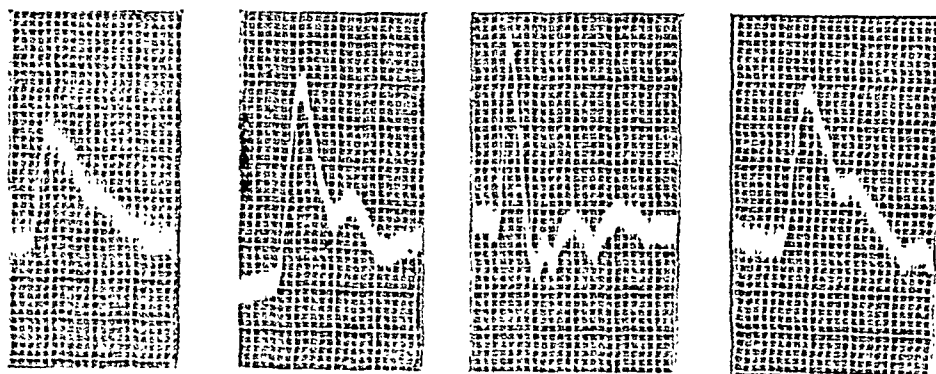
FIG. 5.—The wave-form distortion produced by altering the amplifier values.

The greater the intensity of the light transilluminating the vascular bed, the greater will be the resultant fluctuations and hence the amplitudes of the wave-forms recorded. The other factor controlling this feature of the wave form is the force of the heart beat. Thus, if one could standardize the amount of light actually transilluminating every vascular bed, one could interpret the amplitude of each complex in terms of heart force. Now in transilluminating,

say, a finger-tip, the light has to pass through skin, fat, fascia, vessels, nerves, and bone. All of these, excepting the vessels with their rhythmical alteration in blood content, are constants throughout the period of record taking, but vary from individual to individual. Thus by constructing a direct current photometer recording on a milliammeter, the intensity of the light may be altered so that the same quantity of filtrate is obtained in every case. This amount was decided upon arbitrarily, but with the following provision. There is a tendency for the lamp to become quite warm, and owing to its proximity to the tissues to heat them in turn, so that a local vasodilatation results which is pure artifact. To reduce this difficulty, a focusing light described above was used, and before the standard quantity of light was chosen a series of tests was performed with a thermometer in position over the iris diaphragm. However, there have been occasional cases, especially those in which peripheral vascular disease was present, when an increased amount of light was necessary, and reflected light from a mirror had to be used in these to avoid local heating. The electrical circuit for this photometer unit has been shown in the lower half of Fig. 4. The arrangement of the various components of the amplifier panel board is indicated in Fig. 6.
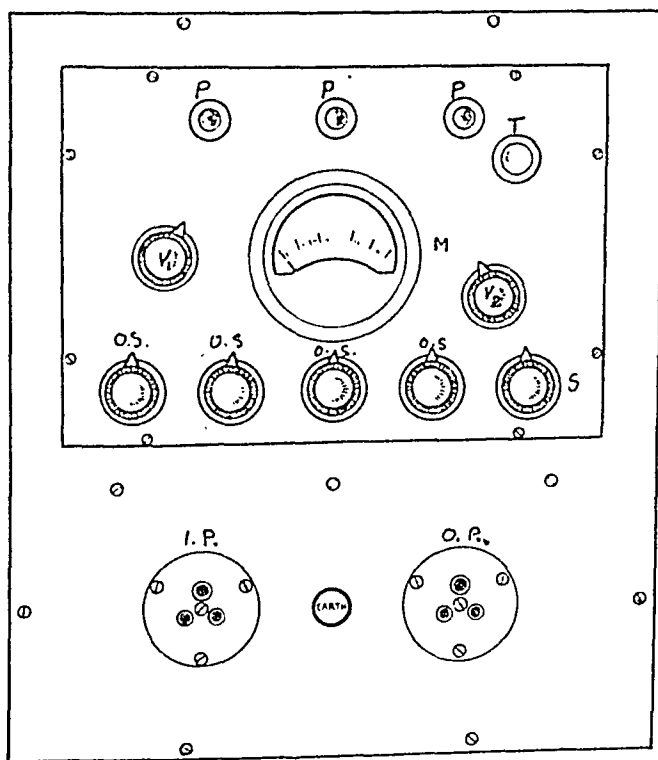
FIG. 6.—The amplifier panel board.
P, pilot light ; M, milliammeter ; T, test button ; V_1, variable resistance photometer circuit ; V_2, variable resistance amplifier circuit ; I.P., input plug ; O.P., output plug ; S, shunt switch ; and O.S., on-off switches.

Method of taking the Records

The procedure for taking records is first to carry out the light calibration. The photometer circuit is switched on and, by means of the variable resistance control, a constant current of one milliampere is employed. The light and photo-electric cell are then brought into the circuit with the tissue to be transilluminated in position. The intensity of the light, the position of the lamp, and the size of the aperture in the diaphragm are altered to suit the designated standard that is specific for each instrument. The photometer is then switched off and the amplifier turned on. The amplifier has in its circuit a standard cell system, similar to that employed for adjusting the tension of the galvanometer string in the electrocardiograph, and so the same amplification is always obtained. The lead from the amplifier is inserted into the socket for the cardiographic leads, and the procedure from here is the same as for an ordinary electro-cardiogram. A protective shunt is incorporated in the amplifier unit to prevent excessive deflection of the galvanometer string during the preliminary adjustments.

RESULTS OBTAINED

Illustrations of the tissue circulation records obtained in normal subjects and in several pathological states follow. Each normal complex consists of a major systolic wave followed by a secondary diastolic wave (Fig. 7 A). In a continuous record sinus arhythmia may be observed, and this is apparent, not only as a change in the rate of the heart, but also as a corresponding change in the force of the heart, which is manifested by alteration in the height of the systolic waves. This is illustrated in Fig. 10 also.

Fig. 7 B shows the effect of excitement and moderate exercise on the normal
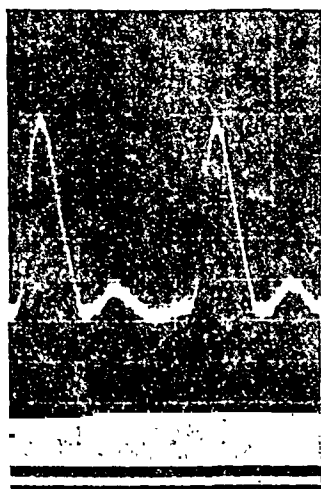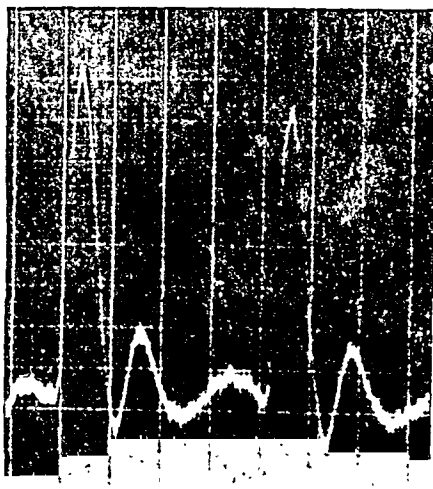
A   B

FIG. 7.—(A) Normal tissue circulation record. (B) Record after exercise.

wave-forms. The heights of both the systolic and diastolic waves are increased, and a third wave makes its appearance in the presystolic period.

Fig. 8 A was obtained after holding the breath for forty-five seconds. It is interesting to see that the diastolic wave still maintains its force in spite of a weakened systolic beat.

Vasodilatation had a marked effect on the tissue circulation record. Amyl nitrite was inhaled and after three minutes Fig. 8 B was taken. There was a great increase in the wave excursions, especially the diastolic one, as there was after exercise.

A normal hand was bathed in water at a temperature of 60° C. and Fig. 8 C taken. The vasodilatation was not nearly so marked as in the previous record.

A   B   C
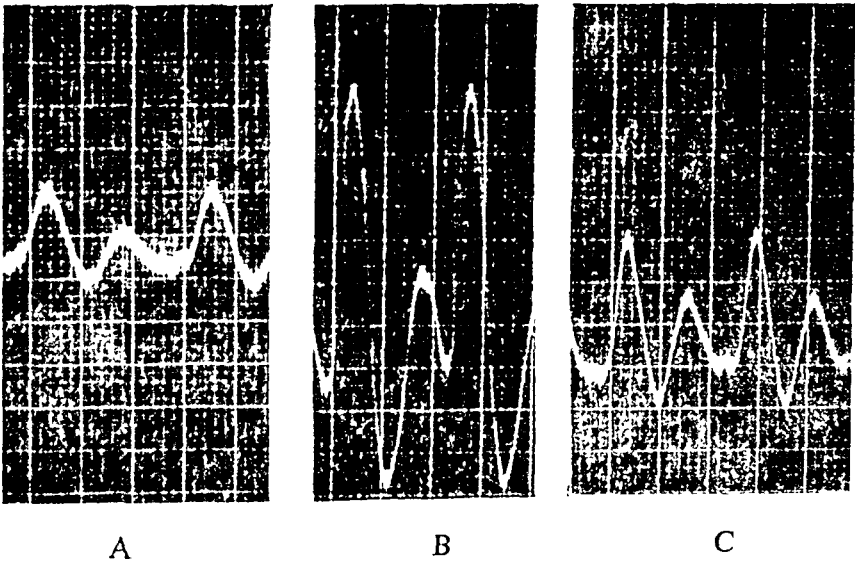
FIG. 8.—(A) Tissue circulation record in asphyxia. (B) Record after amyl nitrite.
(C) Record after vasodilatation due to application of local heat.

Pulsus Bigeminus, Pulsus Alternans, and Pulsus Paradoxus.—Several varieties of pulse rhythm have been recorded. A curve of a typical pulsus bigeminus,

FIG. 9.—Tissue circulation record of pulsus bigeminus.

from a case of digitalis poisoning, shows that the normal beat and extrasystole are coupled and that the extrasystole is a weaker beat (Fig. 9).

An early pulsus alternans is seen in Fig. 10, taken from a case of acute
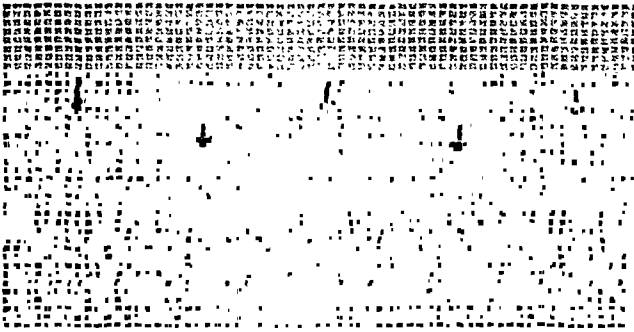
FIG. 10.—Tissue circulation record of pulsus alternans.

rheumatic heart disease. Actually in this record the weaker beat is not linked with the succeeding stronger one, but the variation in force between the beats is only 25 mm. mercury.

Pulsus paradoxus from a case of constrictive pericarditis is shown in Fig. 11 ;
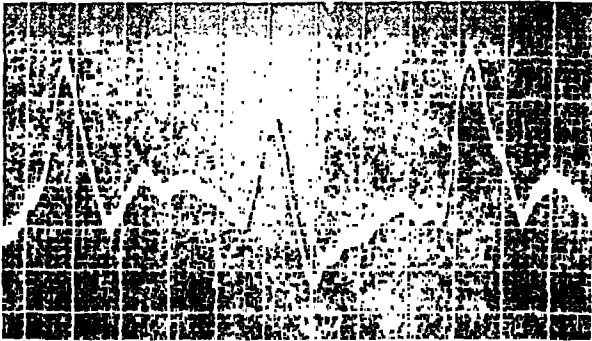
FIG. 11.—Tissue circulation record of pulsus paradoxus.

the weak beat always coincided with the height of inspiration. This is evidence of a constrictive band of fibrous tissue at the base of the heart interfering with its adequate filling during this phase of respiration.

Aortic Regurgitation.—A typical Corrigan or water-hammer pulse is illustrated in Fig. 12, taken from a patient with aortic regurgitation and an aneurysm. The mathematical equation for this wave-form is—

$$\frac{d^2 \log y}{dx^2} = 1 - y \quad \text{where} \quad Y \max = 2.$$

It is hoped that in a subsequent paper formulæ may be evolved for the other records, by which it may be possible to estimate the relative efficiency at which the heart is performing in the different lesions affecting it. Noteworthy in this record is the presence of sinus arhythmia affecting heart force as well as rate.
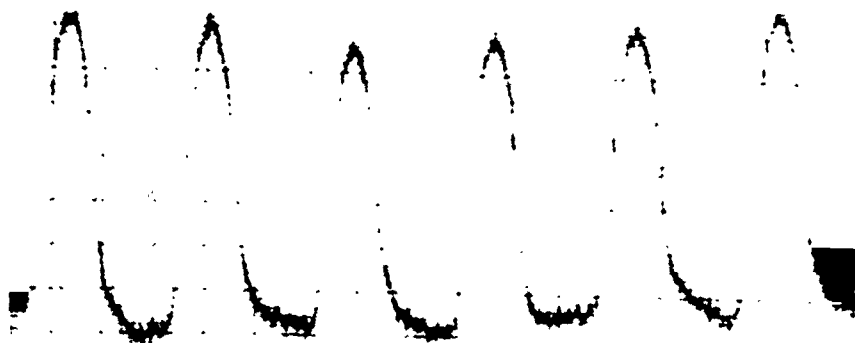
FIG. 12.—Tissue circulation record of a Corrigan pulse.

Auricular Fibrillation.—Fig. 13 is from a patient with auricular fibrillation ; the inconstant heart force is observed as well as the irregular rate.   The longer
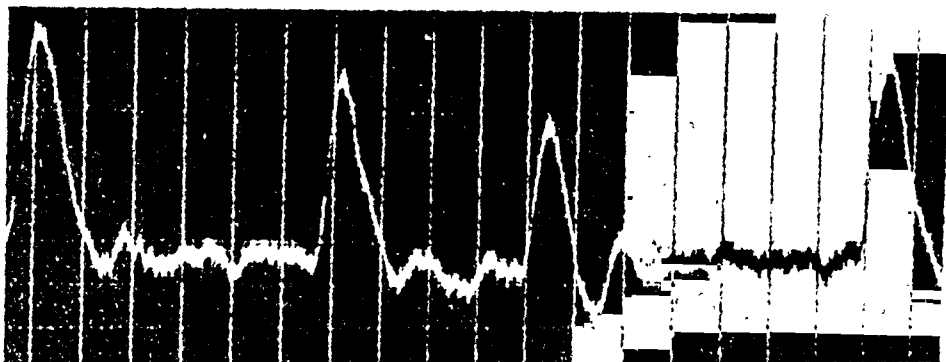
FIG. 13.—Tissue circulation record of auricular fibrillation.

the interval, the stronger the subsequent beat. This patient had a pulse deficiency at the radial artery of 20 beats per minute, but all the beats were readily picked up in the tissue circulation record by transilluminating the thumb.

Myocardial Failure.—In cases of myocardial degeneration with congestive failure, records such as Fig. 14 are obtained. Here there is normal rate and rhythm, but irregularity in the heart force and absence of a diastolic wave. This absence is seen again in Fig. 15, from a patient admitted in a state of collapse, with a diagnosis of coronary thrombosis.
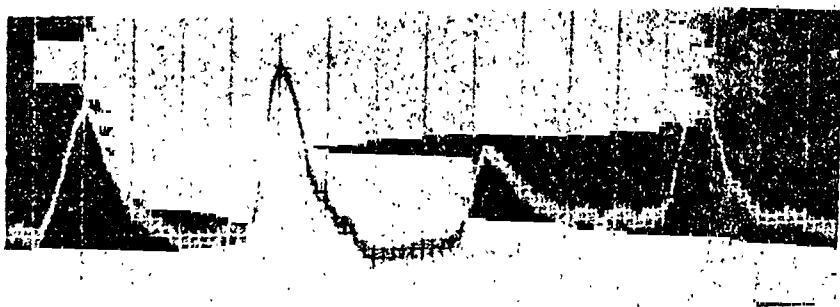
FIG. 14.—Tissue circulation record from a case of congestive failure.
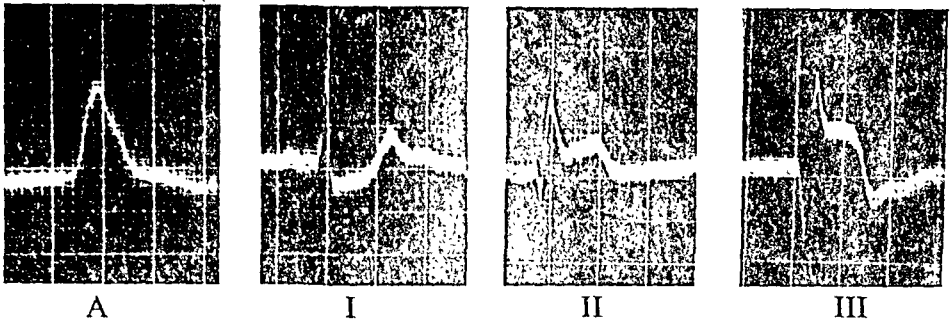
FIG. 15.—Tissue circulation record from a patient with coronary thrombosis (A) and leads I, II, and III of the electrocardiogram.

Fig. 16 is a tissue circulation record (A) and electrocardiogram of a patient with bradycardia due to heart block. The pulse was slow and sustained. His record shows a plateau-topped systolic impulse, but no diastolic wave.
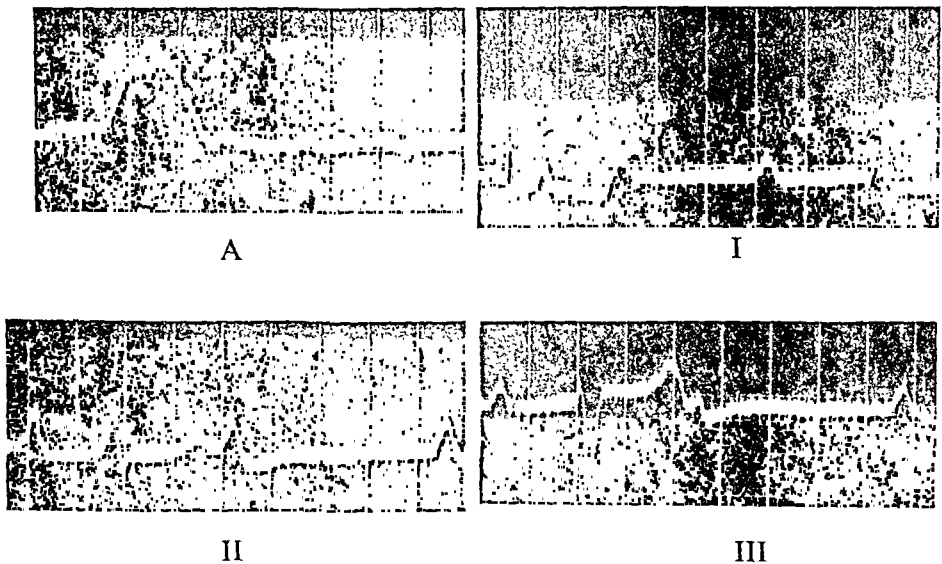
FIG. 16.—Tissue circulation record and leads I, II, and III of the electrocardiogram from a patient with complete heart block.

Peripheral Vascular Disease.—Fig. 17, obtained by transilluminating a finger, the tip of the left hallux, and the right hallux, illustrates the different states of tissue circulation in a man who suffered from obliterative peripheral vascular disease. There were no symptoms in the arms, and the left leg was considered normal, but the right foot was in a state of early dry gangrene. Comparison of the records shows that the left foot was only just on the threshold of normality and suggests that unless an adequate regime of treatment should be instituted, it too would become gangrenous.

The " Pavaex " glass boot has been recommended as an aid to establishing some collateral circulation. Fig. 18 A is a record from the base of a toe that
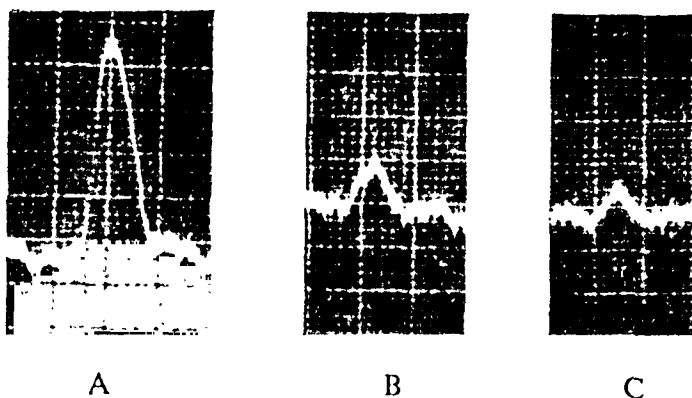
Fig. 17.—Tissue circulation record from a patient with peripheral vascular disease.
(A) From finger.   (B) From left hallux.   (C) From right hallux.

was involved in senile gangrene.   The boot was applied for a period of three hours and Fig. 18 B indicates the state of the circulation two and a half hours after its installation, and Fig. 18 C six hours after it had been removed. Fifteen hours later Fig. 18 D was taken and shows that the improvement was not maintained.
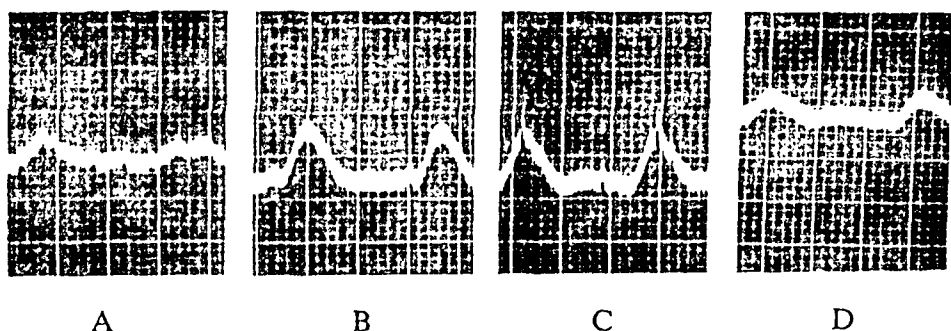
Fig. 18.—Records showing the effect of the " Pavaex glass boot " in producing temporary improvement in the circulation.
(A) Before treatment ;   (B) during treatment ;   (C) six hours after ;   and (D) fifteen hours after treatment.

Measurement of Pulse Velocity.—By superimposing a normal electro-cardiogram on a tissue circulation record, one can accurately time the interval between the electrical response of the apex beat and the appearance of the pulse in the tissues.   This is done by joining the amplifier lead with that from the electrodes on the limbs, and thus a wave-form is obtained which is the resultant of the two sets of records ;   an example is shown in Fig. 19.   While the detail of these forms is now masked, the apex of the R wave of the QRS complex is clearly visible, as is the apex (A) of the systolic wave of the circulation record.   This R–A interval can be measured in the same way as one would measure a P–R interval in the cardiogram.
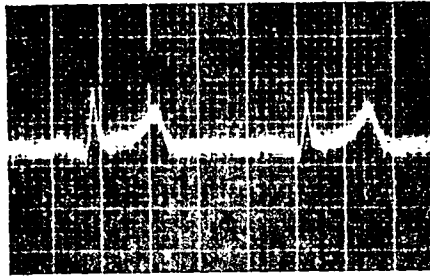
FIG. 19.—Record showing the time of the impulse conduction from apex to tissues.

It is hoped that in the near future it will be possible to publish separate papers with clinical details on some of the records that have been taken. In the meantime, these records have been presented to illustrate the possibilities of the instrument described and to serve as a guide to others who may carry out their own investigations.

SUMMARY AND CONCLUSIONS

1. An instrument for recording vascular changes in the tissues of the extremities and of the body surface has been described. Calibration has been made possible by the introduction of a photometer circuit; results are therefore both qualitative and quantitative. In addition an accurate estimation of the pulse velocity may be made by superimposing the electrocardiogram on the tissue circulation record.

2. The amplifier circuit described is relatively free from electrical distortion and mechanical and physical artifact have been controlled by adequate insulation. The instrument is self-contained and readily portable, and records may be taken without any previous preparation of the patient.

3. A series of typical records has been presented and briefly described. Some of these illustrate physiological reactions to different stimuli, such as heat, excitement, asphyxia, and vasodilatation after amyl nitrite inhalation. The remainder of the records were obtained from cases of certain cardiovascular conditions. Examples of pulsus bigeminus, pulsus paradoxus, pulsus alternans, and the Corrigan pulse have been illustrated. Comparative estimation of the circulation in each of the limbs of a patient suffering from peripheral vascular disease has been included and the effect of the " Pavaex glass boot " has been demonstrated.

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REGENERATION IN CARDIAC MUSCLE

BY

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Proliferation of striated muscle, either in the form of regeneration of damaged tissue or *hyperplasia* of relatively normal cells, is generally thought not to occur. Such an opinion is an example of the general idea that more " specialized " tissues differ from less " differentiated " tissues in that they are unable to multiply in adult life.

This proposition, however, has gradually become more and more untenable during the past fifty years. At an early stage in the development of microscopy the capability of various forms of epithelium—skin, alimentary canal, etc.— for proliferation was appreciated. For some time such capacity was denied the more " specialized " epithelia such as the liver and renal cells. When hepatic and renal proliferation was at last recognized, the original view was still applied to other tissues, notably muscular and nervous cells.

Whether one regards a mucous cell of the intestine as being more differentiated than a fibrous tissue cell and less differentiated than a liver cell is purely a question of the point of view from which it is considered. The intestinal cell cannot, or in ordinary circumstances does not, produce collagen fibres, nor the liver cell mucin. Apart from this question and the presumed inverse capacity for proliferation, there is no doubt that certain cells may be observed to multiply more often than others. This has been recognized from the earliest days of histological study, but though many cells were thought not to multiply at all, it is now known that, to some extent, they do.

Regarding muscle cells, hyperplasia of smooth muscle was the first observed. More recently, regeneration of voluntary muscle, both naturally and experimentally, has been described, but knowledge of such changes in heart muscle has lagged behind.

HISTORICAL

The question of regeneration of cardiac muscle fibres has often been discussed in the last eighty years. The earliest writers—Kölliker (1852), Friedreich (1855), Paget (1865), von Rokitansky (1856), and Rindfleisch (1867)—accepted without question the occurrence of hyperplasia. Lebert (1857), however, emphasized the absence of any direct histological demonstration. Goldenberg

(1886) reviewed the previous reports and concluded that, though increase of cardiac tissue was largely by hypertrophy of muscle fibres, longitudinal splitting could occur. Zielonko (1875), from observations on the hearts of frogs and rabbits, thought that hyperplasia of cells took place.

Tangl (1889) and Wideröe (1911), and, more recently, Kaufmann (1928), Aschoff (1936), and Mönckeberg (1924) attributed all enlargement of the heart to hypertrophy of fibres without hyperplasia. They based their views mainly on the absence of mitotic figures. On the other hand, Ziegler (1889), Adami and Nicholls (1909), Saltykow (1905), Heller (1913), and Rössle (1923) maintained the probability of hyperplasia, but did not produce incontrovertible evidence of this. Counts and measurements of muscle fibres, however, made by Collier (1922) and Karsner *et al.* (1925) suggested that not only hypertrophy but also hyperplasia occurred.

Thus opinion was divided, and MacMahon (1937), reviewing the position recently, indicated that, since increase in fibres—probably by splitting—had been accepted by many writers, the principal difficulty was failure to demonstrate mitotic figures in muscle nuclei. He described cases in which such had been observed, and the illustrations leave little room for doubt regarding their occurrence in heart muscle of children.

Most of the material that has been studied was heart muscle obtained from various forms of toxic or inflammatory diseases of the myocardium. The muscle changes after injury have been reviewed by Hesse and Hesse (1924) and by Klose (1923). There is the same uncertainty in such cases, though the evidence appears somewhat to favour the occurrence of hyperplasia of muscle cells.

PATHOLOGICAL MATERIAL

The observations that form the basis of this paper were made on the heart muscle in the neighbourhood of a recent wound.

A man, æt. 19 years, received a penetrating knife wound of the chest, which caused a superficial injury to the anterior wall of the left ventricle. The heart was exposed and the wound sutured with silk. The patient recovered from the operation, but died from a streptococcal septicæmia on the fourth day.

A necropsy was performed six hours after death. There were small amounts of blood clot and of sero-purulent material in the anterior pericardial region; this was walled off by soft adhesions from the remainder of the pericardium which was unaffected. The lungs showed some patchy congestion and there was straw-coloured fluid in the left pleural cavity. There was congestion and toxic damage in the liver, kidneys, etc.

Pieces of heart wall were removed from the seat of the injury ; it was healing well but could be recognized by the suture material used at operation.

Microscopically, the muscle cells appeared normal, though striations were indefinite in some areas—attributed to post-mortem change and the general toxæmia. Near the wound edge the muscle cells were separated from each other by fluid (œdema) (Figs. 1 and 2), and this made the examination of

FIG. 1.—Photomicrograph of muscle fibres near area of injury, cut in longitudinal section. The fibres are about half the thickness of those in neighbour··· ·· ··· ····· ·· nd 4). Splitting of fibres may be seen, and they run, more or less, in pairs. Magnification ×350.
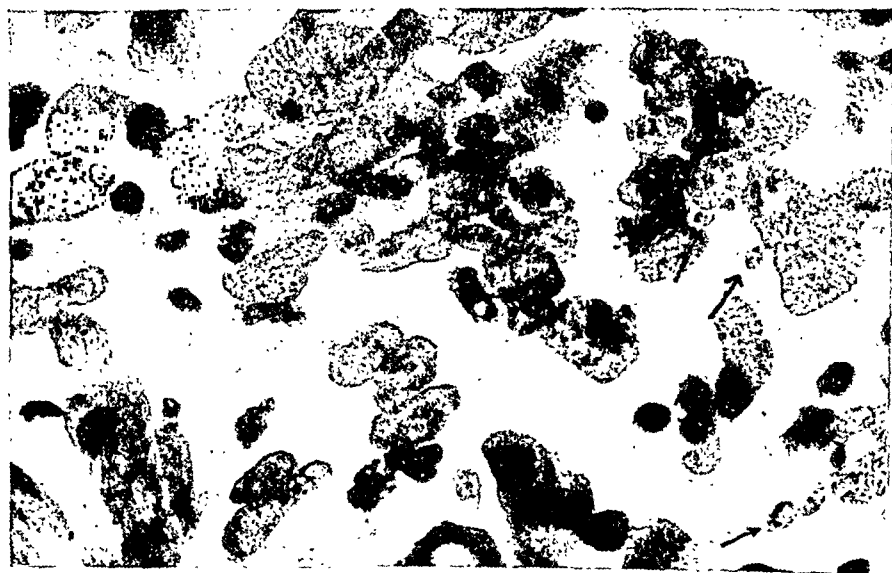
FIG. 2.—Photomicrograph of muscle fibres close to the injured area, cut in transverse section. Some are very small, only about 7μ in diameter (arrows). There is separation of some fibres by œdema and an absence of vessels in some of the groups of fibres. ×350.

L

individual fibres easier than usual.   Immediately adjacent to the injured area the changes in the tissue were maximal.

At the site of injury there were numerous wandering cells of various kinds and many fixed cells with larger nuclei and more voluminous protoplasm than similar cells elsewhere.   Their number steadily diminished in the surrounding tissue until at a distance of about 0·5 cm. the number was minimal and corresponded to that observed elsewhere.   The affected area was arbitrarily divided into three zones : a central one with the greatest damage and greatest accumulation of connective tissue cells, an intermediate one, and a peripheral one where such connective tissue changes were definite and in excess of any seen in the normal myocardium, but less developed than the other zones of activity.

The muscle fibres in the intermediate—and to some extent in the peripheral —zone were much thinner than those elsewhere.   They were arranged in pairs (Fig. 1) or in small groups (Fig. 2), sometimes separated from other similar groups, but at times in larger numbers due to the aggregation of smaller groups. Although blood capillaries were dilated and easily observed, these seemed to be fewer in proportion to muscle fibres than in other parts.   These groups of small fibres were regarded as arising from the splitting of fibres.

In or close to the central zone muscle fibres appeared to end, and in many there was degenerative change of a hyaline type in this area (Fig. 3).   From the ends of such fibres masses of protoplasm containing a number of large vesicular nuclei were observed.   This protoplasm in some parts showed striations.

The nuclei in the fibres varied considerably in size, shape, and staining characters.   In some of the cells there were double nuclei (Fig. 4).   Many resembled the atypical nuclei seen in chronic myocarditis.   A number of very irregular nuclei were found.   Careful search of the fibres showed that in a number of them there were, replacing the nuclei, irregular masses of chromatin, deeply staining and consisting of an aggregation of small chromatin masses and rods (Fig. 5 ; at the top of p. 160).   These appeared to be mitotic figures in various stages of evolution.

DISCUSSION

The case described was chosen partly because the local conditions seemed most suitable (as shown by the rapid proliferation of connective tissue and healing) for proliferative changes in the muscle, and also because such proliferation might be expected more readily in a young than an old subject.

The muscle changes found were of two sorts :

1. Those involving the whole muscle fibre—(a) splitting of the fibres, and (b) outgrowths in the neighbourhood of damaged tissue.
2. Those affecting the nuclei—(a) the presence of double nuclei, and (b) the presence of mitotic figures.

FIG. 3.—Photomicrograph of a section through the end of damaged fibres (showing some degenerative change), in which outgrowth of new fibres is occurring. × 350.

FIG. 4.—Photomicrograph through an area adjacent to the wound showing double nuclei (arrows). ×350.

A   B
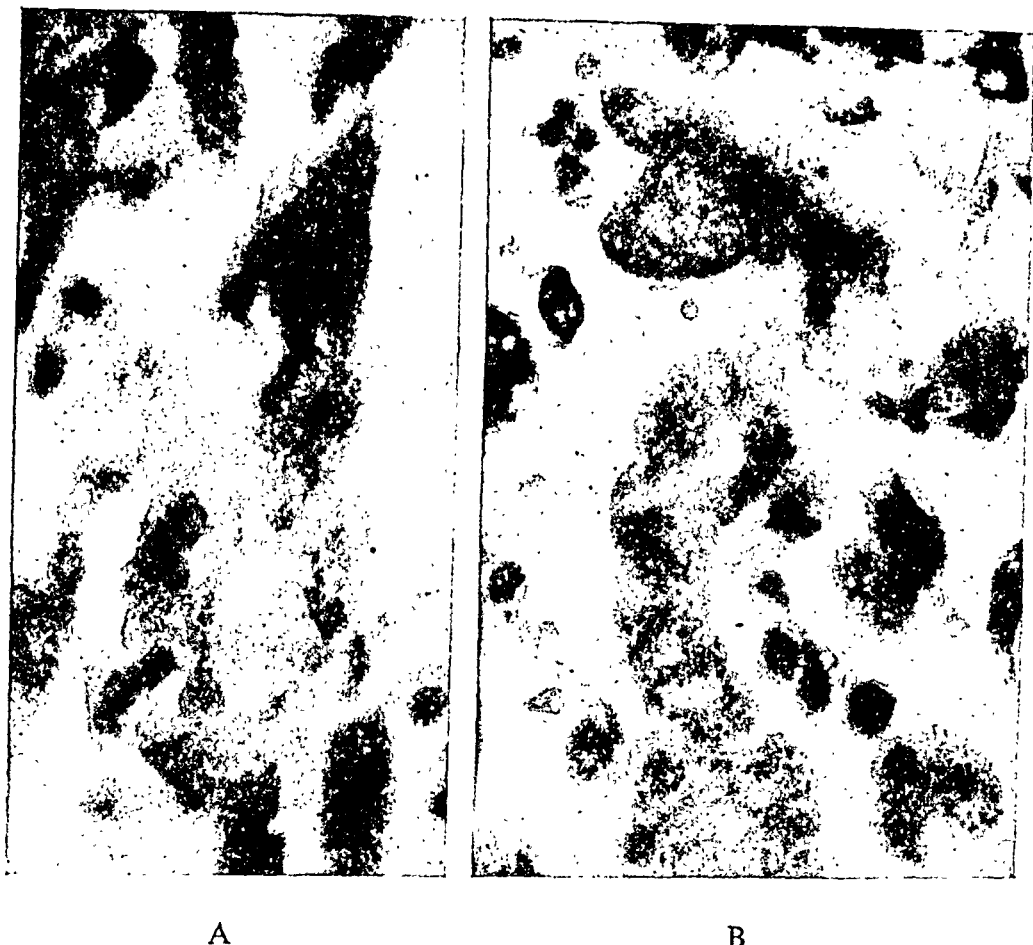
Fig. 5 (A).—Photomicrograph of muscle near the injured area showing a mitotic figure.
×350.   (B).—The same, cut in cross section.   ×350.

1. (a) In cardiac muscle where fibres are of unequal size and where anastomosis of fibres is common, proof of splitting of these fibres is not easy to obtain. However, the fibres in the neighbourhood of the affected area may be compared with those in other parts.   Two observations seem to be of importance in this regard.

Firstly, many of the fibres in the healing area are smaller than those in other parts.   When cut in longitudinal sections they can be seen to run for some distance in pairs (Fig. 1), and in transverse sections the division of the fibre into a number of components can be seen (Fig. 2).   Such appearances, of course, may be found in other parts of the heart, but in the affected zone the small fibres can be seen to be much smaller than those in other areas ; in some cases they are about 7 μ in diameter.   The way in which the fibres split is shown in the diagrams in Figs. 6 and 7.   This is, of course, hypothetical, but was drawn from different sections and shows the way in which a fibre may separate into component parts, and because of the small size of the fibre was assumed to be occurring at the time of death.   It will be seen that the new fibres are formed by separation of groups of Cohnheim's areas.

Secondly, in the normal heart it is easy to demonstrate that there is one capillary for each muscle fibre, but in the affected tissue, although this was not proved by injection of the vessels, such vessels did not appear to be so numerous, and indeed there seemed to be only about half the number of vessels to the same
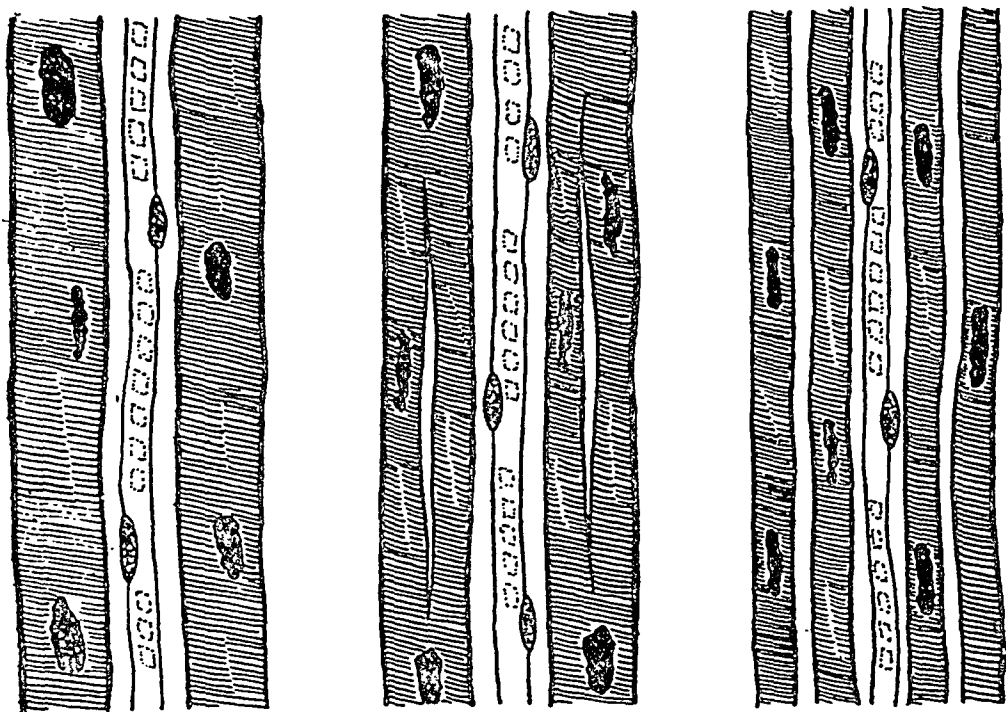
FIG. 6.—Diagram to show the probable method of formation of the new fibres (cf. Fig. 1). Note the relationship of capillaries to fibres.

1.　　　　2.　　　　3.　　　　4.
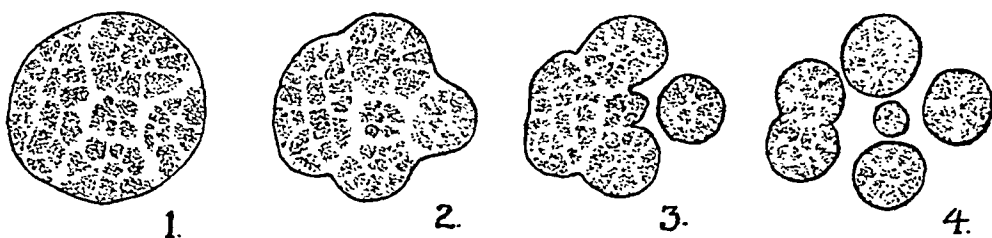
FIG. 7.—Diagram to show the stages of division of muscle fibres, as seen in cross section (cf. Fig. 2). Serial sections through normal tissue will show a similar, though less developed, arrangement at sites of division of fibres.

number of muscle fibres. This arrangement and its mode of development is shown diagrammatically in Fig. 6.

(*b*) In the neighbourhood of damaged muscle tissue there are a large number of cells of different kinds, some wandering and some fixed, most of which are

of connective tissue origin. Some of these cells, recognized largely by the amount of protoplasm and also by its eosinophilic staining characters, have been regarded as arising from muscle cells. The protoplasmic outgrowths, however, from the ends of damaged muscle fibres, particularly since some of them show striations, seem to be attempts at formation of new muscle fibres (Fig. 3).

2. (*a*) In a number of the fibres the nuclei are arranged in pairs ; these lie close together and overlapping, or side by side with their long axes parallel. These have been seen by many investigators and suggest multiplication of nuclei. However, double nuclei occur normally in Purkinje fibres, and one must exclude this possibility before it is assumed that they are in ordinary muscle fibres. This may be suggested by the absence of the other features of Purkinje fibres, but the more certain method is to compare the affected area with relatively normal tissue in the neighbourhood. When this is done it is found that the number of fibres containing double nuclei in the affected zone is greatly in excess of that in the neighbouring tissues.

(*b*) Finally there is the question of mitotic figures. In a number of the cells the nucleus is found to consist of an aggregation of small irregular deeper staining chromatin masses, usually in the form of rods. This area is surrounded by a zone of paler staining protoplasm. In the material examined these mitotic figures were rather irregular and did not show the characteristic features—the aster, diaster, etc.—of normal mitosis. In addition, there were a large number of very irregular nuclei—irregular in contour and much more deeply staining than their neighbours—and though it is tempting to regard these as related to the mitotic figures, this could not be proved. They closely resemble the irregular nuclei observed in cases of cardiac hypertrophy and chronic myocarditis.

Thus we have, in this damaged tissue, changes in the muscle cells which suggest that proliferation is taking place to some extent. There is indubitable evidence of nuclear activity, and the cells are undergoing hyperplasia in two ways—partly by protoplasmic outgrowths in the region of injury, and partly by splitting of fibres and the formation of new ones.

It is not intended to suggest that such proliferation of muscle plays a predominant part in the healing of an injured area ; there can be no doubt that healing occurs by connective tissue activity and the formation of a fibrous scar. It is merely intended to indicate that muscular hyperplasia, which is often considered to be absent, does occur to some variable extent.

SUMMARY

1. Examination of a recent heart wound in a young adult was undertaken to determine the possible presence of myocardial hyperplasia.

2. This was demonstrated by :

    i. The splitting of the fibres—as indicated by the size and arrangement of the fibres and their relationship to the capillary vessels.

ii. Protoplasmic outgrowths from the ends of damaged fibres.

iii. The presence of double nuclei in some fibres.

iv. The presence of mitotic fibres.

3. This does not, however, presuppose that such hyperplasia is responsible for the healing of wounds, which occurs by the usual connective tissue proliferation and by the formation of scar tissue.

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EDITORIAL NOTE

The general consensus of opinion is that hyperplasia of cardiac muscle does not take place. The subject was well reviewed by Karsner, Saphi, and Todd (1925) in adults and by McMahon (1937) in children. The editors have, however, decided to publish this paper as the subject's death so soon after the injury to his heart provided an unusual opportunity of re-examining the question, and the author has presented the evidence for his point of view fairly and scientifically. None of the points on which he bases his opinion seems to the editors to be final or conclusive, and the question is complicated by the actual cause of death from septicæmia, with the possibility of resultant changes in the nuclei. Thus the splitting of fibres and their apparent arrangement in pairs might possibly be an artefact ; the protoplasmic outgrowths and many of the changes seen in the nuclei might be the result of the infection and of degeneration ; the double nuclei might be Purkinje fibres (though the author considers this improbable) or might be due to the superimposition of two nuclei. It is

only fair to add that the author has considered these explanations and rejected them ; but the evidence seems inconclusive to the editors.

The two conclusive pieces of evidence would be a cell count, which is admittedly very difficult in cardiac muscle, or the presence of mitotic figures. The author thinks these last were observed, but admits that they were atypical, and the picture of mitosis with its spindles and regular formation is very unmistakable.   Should a similar case occur with death resulting directly from the effects of the accident elsewhere without the complication of infection, an ideal opportunity of re-testing the question would be provided.

TUBERCULOUS PERICARDITIS

BY

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In Europe tuberculous pericarditis is uncommon as a primary clinical manifestation, even in the constrictive form that is suitable for operative treatment (White, 1937). Observation over fifteen years in the Non-European Hospital, Johannesburg, has shown that here it is not rare as a primary clinical entity. In this series of 31 cases some were of this type and some were only part of a generalized tuberculæmia ; there were none of the healed constrictive type.

The importance of the first type is that we have found it amenable to treatment. Unfortunately, Bantu patients are difficult to keep in hospital for long and almost impossible to follow up.

Some fifteen years ago a case was seen with œdema of the left arm and of the face, without albuminuria. There was pyrexia, but no classical signs of heart failure. The increased area of cardiac dullness suggested a pericardial effusion and the pear-shaped shadow with an obtuse cardio-hepatic angle was confirmed by radioscopy. Repeated pericardial punctures found no fluid. Autopsy showed that the pericardial sac was occupied by caseous material of great thickness, the myocardium being reduced to a thin sheet. Other somewhat similar cases were seen ; a single puncture only was done in some and fluid was absent. In 1938 a number of such cases were seen by both of us, differing only in that many of them had effusions, so that confirmation of the diagnosis by direct and biological methods could be made. Few of these later cases showed what had been considered the cardinal clinical sign, viz. œdema of the arm or face.

They were generally admitted as cases of congestive heart failure. There was an intermittent, remittent, or irregular fever. The shape of the heart could generally be outlined at the bedside accurately enough to differentiate it from the heart of beri-beri or from rheumatic or syphilitic heart disease with failure. Rheumatic pericarditis with effusion is very rare in these people (though the dry variety is not uncommon), so the finding of a large " pericardical-shaped heart " in a Bantu justifies a clinical diagnosis of tuberculous pericarditis, when rheumatic manifestations and evidence of mitral and aortic disease are absent.

The area of cardiac dullness sometimes attained huge proportions and in one case extended almost from axilla to axilla and yielded over a pint of fluid on

aspiration. The heart sounds were usually muffled and murmurs were absent. In some cases a pericardial rub was heard. The pulse was generally rapid, 90–120, and a pulsus paradoxus was occasionally present. Extrasystoles and fibrillation were rare.

The signs in the lungs were generally those of congestion, and our series showed that the presence of pulmonary tuberculosis as a clinical entity was not necessary for the diagnosis of the condition. In the differential diagnosis the association of pulmonary tuberculosis and congestive heart failure should make one consider the question of tuberculous pericarditis. Pleural effusions were frequently found and were often bilateral.

Symptoms were vague, as might be expected in a primitive people, not able to describe their feelings accurately. In some cases there was precordial pain, and abdominal pain was common and was usually localized to the right hypochondrium, due to the acutely tender liver of recent rapid cardiac failure. The other symptoms were those common to cardiac failure.

Confirmation of the clinical diagnosis was often made at autopsy and in others by biological examination of the pericardial. fluid. This fluid was sometimes serous, but most often hæmorrhagic. In several cases fluid could not be obtained and subsequent autopsy showed caseating material only.

The radiographic findings confirmed the cardiac enlargement and showed an obtuse hepato-cardiac angle. A typical illustration is given in Fig. 1. In
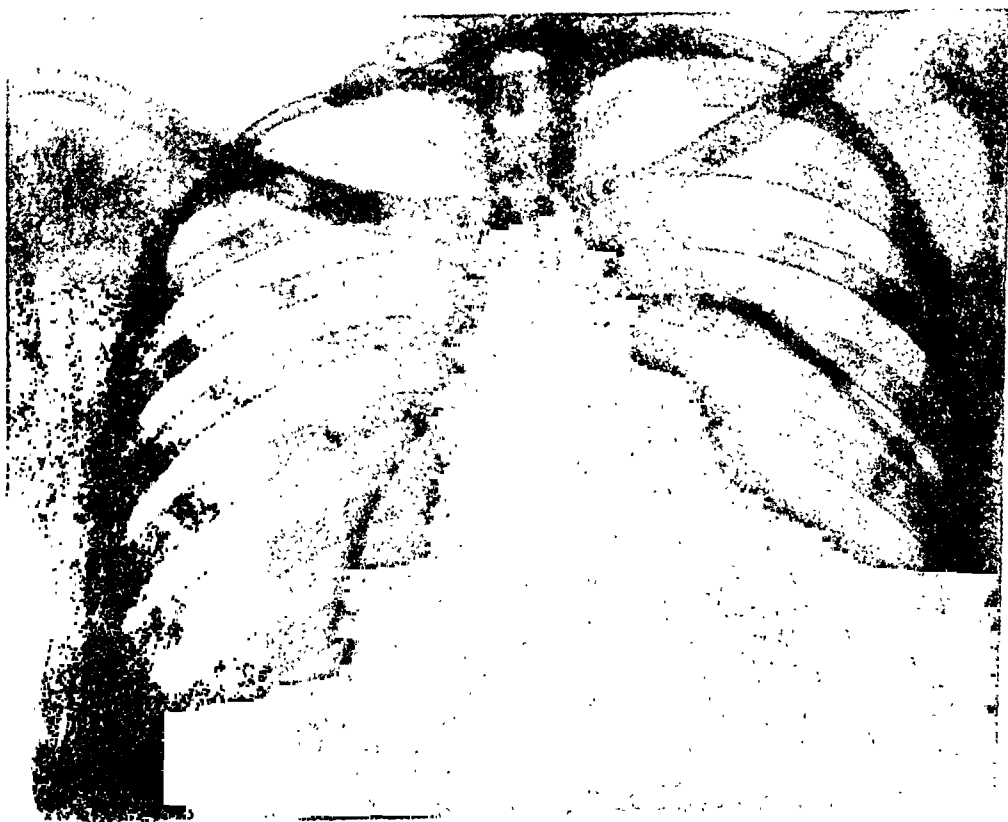
FIG. 1.—Routine teleradiogram showing the hydro-pneumo-pericardium.

three cases kymographic tracings were obtained by the courtesy of Dr. Weinbren and Dr. Meyer. One after pneumopericardium is shown in Fig. 2. It was

FIG. 2.—A kymogram taken with a moving grid in one second. The cardiac pulsations in the portion surrounded by air are well marked. Note that the peaks on either side of the pericardium are not opposite each other.

taken with a moving grid in one second. The long lines at the junction of air and fluid are due to splashing of the fluid. The cardiac pulsations in the portion surrounded by air are well marked, but below the level of the fluid they cannot be detected, either because of the density of the fluid or because the cardiac pulsation is damped down. In this case even if the cardiac pulsations were not damped down by the fluid, the density of the fluid would still have obscured them. The thickened pericardium itself shows transmitted pulsation. The kymogram of another case is shown in Fig. 3, where the pericardial effusion has completely damped down the pulsations of the heart itself.

In this series, dating 1925–1938, 31 cases were found in the records of the hospital, and of these 10 were seen in the first half of 1938. The cases diagnosed clinically were those with the picture described above. The others were part

FIG. 3.—A kymogram taken in inspiration. Pulsations can be detected in the great vessels.
The pericardial effusion has completely damped down the pulsations of the heart itself.

of a generalized tuberculosis and are included for the purposes of discussion
as to the path of infection and pathological development of the condition.
Some of the latter were of the adhesive type, but being part of a generalized
tuberculæmia were not referred to the surgeons.

DESCRIPTION OF CASES

The nature of the condition and its progress have been a source of con-
jecture to some authors. In common with others, we believe that it begins
acutely, then passes into a stage of effusion or caseation, and finally develops
an adherent stage.

For the purposes of description our series is divided into three groups :

(1) Those with a normal area of cardiac dullness ;
(2) Those with a greatly enlarged area of cardiac dullness ; and
(3) Those passing through various stages of the condition.

(1) Cases with a Normal Area of Cardial Dullness

This group comprises 9 cases with an adherent pericarditis, as a result of which there was obliteration of the pericardial sac.

Sex and Age.—There were 6 males and 3 females. The age limits were between 15 and 76 years.

Histories.—These varied, particularly in regard to the patients' chief symptom. There was a cough in all cases, but only once an hæmoptysis. The other symptoms were chest pain, frequently over the precordium (4),* breathlessness (2), œdema of the legs (2), and a generalized œdema, involving the face, arms, and legs (1) ; abdominal pain, usually localized to the right hypochondrium (4), diarrhœa with the passage of blood-stained stools (2), swellings situated over the sternum (2), and loss of weight (7).

Temperature and Pulse Rate.—Febrile charts were present in 6, the fever being either intermittent or remittent in character.

The pulse rate was increased in 8 ; auricular fibrillation was present in 1, and this was the only irregularity. The respiratory rate was increased in 4 ; in 2 others occasional attacks of breathlessness occurred.

Clinical Signs. Cardiovascular.—Slight cardiac enlargement to the left was found in 2 ; in neither of these did the outline of the area of cardiac dullness suggest a pericarditis with effusion ; 1 had an increased area of cardiac dullness, which later, however, became normal. Normal heart sounds were found in 7. Bilateral pleural effusions were present in 2, and in 1 there was a left-sided effusion.

Abdominal.—Generalized abdominal tenderness was found in 1, and in 2 the abdomen had a doughy feel. Ascites was present in 5, the liver was enlarged and tender in 2, and irregular abdominal masses were present in 1 other.

Autopsy.—An adherent tuberculous pericarditis was present in all. Extra-pericardial adhesions between the pericardium and surrounding organs were only found in 1—in this instance between the pericardium and the chest wall. Slight cardiac enlargement was present in 3. Tuberculous infiltration of the myocardium was found in 3, in 2 of which it was generalized, involving both auricles and ventricles, and in the other it was localized to the right auricle. Pulmonary tuberculosis was found in 5, including 1 with a commencing tuberculous broncho-pneumonia. In all the others œdema and congestion of the lungs were present. The outstanding feature was that in all cases the root glands were tuberculous.

Generalized abdominal tuberculosis was present in 2. A tuberculous abscess of the chest was present in 1. Pulmonary infarcts were present in 1 case.

The diagnosis in this group is much more difficult than in the subsequent group. Very few cases in this group showed signs of cardiac failure. Pathologically the adhesions which formed were usually intra-pericardial and very rarely extra-pericardial.

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* The numbers in brackets indicate the number of patients with this symptom.

(2) Cases with a Greatly Enlarged Area of Cardiac Dullness

This group is made up of the 19 cases with either a serous, hæmorrhagic, or caseous exudate in the pericardial sac on the one hand, or those with loculation of the fluid due to adhesions between the visceral and parietal pericardial layers on the other hand. Loculation was proved, usually at autopsy, and indicated the start of the adherent stage.

Sex and Age.—There were 5 females and 14 males. The age incidence varied between 19 and 60, the commonest age being between 20 and 40 years.

Histories.—The duration of illness varied from a week to three years, the commonest period being about three months. Cough was complained of in 18 cases ; one had an hæmoptysis and three others had at times coughed up blood-stained sputum ; in one of the latter, it was found that she had had pneumonia. In 7 there was a history of pain (5 precordial and 2 right-sided). Breathlessness on exertion was noted by 13 patients, and 10 complained of œdema of the legs.

Swelling of the abdomen was found in 3 and abdominal pain in 10, usually localized to the right hypochondrium. Loss of weight, very marked in some instances, occurred in 9 ; only 2 complained of night sweats.

Temperature and Pulse Rate.—Remittent or intermittent fever occurred in 14.

The pulse rate was raised in 17, and pulsus paradoxus was found in 2. The respiratory rate was increased in 16 cases.

Clinical Signs.—Œdema of the legs was present in 7, and one of these had œdema of the face in addition. 13 had evidence, in some instances very marked, of wasting.

Cardiovascular.—The apex beat was palpable in 1 only. Gross enlargement of the area of cardiac dullness was found in 17. Pleural effusions obscured the cardiac outline in 2, and in some cases the area of dullness extended from axilla to axilla. The area of·cardiac dullness was in most instances characteristically pear-shaped, with an obtuse cardio-hepatic angle. In all cases the heart sounds were normal, but generally muffled and distant. The types of pericardial effusions found will be dealt with under pathology.

Respiratory.—Signs indicating the presence of pulmonary tuberculosis were found in 5, the commonest clinical signs being an impaired note at one or both apices, with moist sounds in the chest. Bilateral pleural effusions were present in 2, whilst 3 had right-sided effusions. In 2 a left-sided pleural effusion developed after aspiration of the pericardium.

Abdominal.—An enlarged and very tender liver was found in 10, and 3 had ascites.

Pathology or Autopsy.—Autopsies were carried out in 16, and tuberculous pericarditis with effusion was present in all. In one just over four pints of effusion was present, whilst in others as little as 30–50 c.c. were found. In 7 the effusion was purely hæmorrhagic, in 5 caseous, and in 2 serous. Mixed types of effusion were present in 5 cases ; 3 hæmorrhagic and caseous ; 1 hæmorrhagic and fibrinous ; and 1 caseous and serous. In 6 the effusion was found to be loculated by intra-pericardial adhesions. In 7 the heart was found to be small. Slight cardiac enlargement was found in 1, and 1 had a bread-and-

butter heart. Tuberculous infiltration of the myocardium was present in 6 ; the right auricle being involved in 3, a generalized involvement in 2, and involvement of the left auricle in the other. Active pulmonary tuberculosis was present in 8, and in the remaining 8 the lungs were œdematous and congested. An infarct of the right basal lobe was present in 1 case. Here, as in the previous group, the root glands were tuberculous in every case. Pleural effusions were present in 10 (8 bilateral, 1 right-sided, and 1 left-sided). The liver was tuberculous in 7 and the kidneys in 7. In 3 the spleen was tuberculous, and in 3 the intestine. Tuberculous mesenteric glands were present 4 times.

Treatment in our cases consisted of pericardial aspiration and the use of mercurial diuretics and digitalis. Later we began using the method of pneumopericardium. Two who had pericardial aspiration left hospital in a much improved condition. Pneumopericardium was carried out in two cases, one of whom died, whilst the other left hospital much improved.

Remarks.—Of the 19 patients reviewed above, 7 were seen by us in six months, and all were diagnosed clinically and confirmed biologically or by autopsy. They were usually admitted with the diagnosis of congestive cardiac failure, but a thorough examination and certain features, such as the febrile chart, the enlarged and pear-shaped area of cardiac dullness, the atypical distribution, and order of occurrence of the œdema, pointed the way to the correct diagnosis. The presence of a pericardial effusion is responsible for the picture of congestive heart failure as found in most cases. The effusion, as we have seen, may be either hæmorrhagic, serous, caseous, or a mixture of two types, the hæmorrhagic being the commonest. Loculation of the effusion due to intrapericardial adhesions may be present. Tuberculous infiltration of the myocardium was most commonly found in those cases with a caseous effusion. A feature of these cases was the absence of signs of pulmonary tuberculosis in most instances. Thus these cases fall chiefly into the clinically primary type of tuberculous pericarditis.

(3) Cases passing through the Various Stages of Tuberculous Pericarditis

The three cases in this group are important in helping to elucidate the course of tuberculous pericarditis. They demonstrate the passage of the condition through an acute stage to an effusion stage, and finally to the adherent stage.

Sex and Age.—All were males. Their ages were 26, 40, and 50 years respectively.

Histories.—The duration of their illness prior to admission was one, three, and eight weeks respectively. Breathlessness on exertion and œdema of the legs were complained of by one patient. All complained of cough, but none had had an hæmoptysis. One had precordial pain, and all abdominal pain.

Temperature and Pulse Rate.—Intermittent fever occurred in two, whilst the temperature was normal in the third.

The pulse rate was increased in all, and the respiratory rate was normal in all.

Clinical Signs.—Marked loss of weight was evident in two. Œdema of the legs was present in one.

Cardiovascular.—One had systolic apical retraction, and in two there appeared to be cardiac enlargement to the left. A pericardial friction rub was present in all three. This disappeared later in one. The heart sounds were normal.

Respiratory.—An impaired note with broncho-vesicular breath sounds was present in one at the right apex ; emphysema was found in one, and moist sounds were present in one throughout both lung fields.

Abdominal.—An enlarged and tender liver was found in one case, whilst the abdomen was generally tender in the other.

Autopsies.—A hæmorrhagic pericardial effusion loculated by intra-pericardial adhesions was present in one. An adherent pericarditis was present in the other two and in one of them extrapericardial adhesions, a rare finding, were present between the heart and lungs. Tuberculous infiltration involving the right auricle existed in one. The root glands were tuberculous in all. Pulmonary tuberculosis was present in all, one having a tuberculous broncho-pneumonia with a terminal miliary spread ; in one, however, it was due to a direct infiltration from the root glands. The spleen and liver and the abdominal and cervical glands were tuberculous in one.

The outstanding feature in these cases was the presence of a pericardial friction rub. This is highly indicative of an acute stage of the condition. In the first particularly, one was able to follow the condition through the acute, effusion, and commencing adherent stages.

Summary of the Three Groups

Incidence.—The coloured races are more commonly affected than the Europeans. Tuberculous pericarditis is more common in males than in females, 23 to 8 in this series. The difficulty in assessing the age incidence lies in the fact that the non-Europeans in this country rarely know their correct ages. The impression we have gained from this series is that the condition is commonest between the ages of 20 to 40 years and the ages given coincide with this ; cases, however, occurred from the age of 15 to the age of 76.

Pathology.—It is of considerable importance that in all the 28 cases with autopsies, the root glands were tuberculous. We think that these glands are the commonest source for the spread of tuberculous infection to the pericardium.

The Manner in which Tuberculosis reaches the Pericardium

There are three modes of spread :

(1) *Spread by Direct Contact.*—This is very rare and cannot be demonstrated in our series. It is, however, a possibility where tuberculous lungs or glands lie in direct contact with the pericardium. One would, then, expect to find the tuberculous process continuous with the adjacent focus, and spread throughout the parietal pericardial layer, but this is very rare and the probability is that even in these cases the spread takes place via the lymphatics.

(2) *Spread by the Blood Stream.*—This is a more common mode and usually

occurs in the terminal miliary spread of a pulmonary tuberculosis. Miliary tuberculosis is a more common sequel of tuberculous pericarditis than vice versa. Not one case in this series resulted from a terminal miliary spread, whereas eleven cases of root gland and pericardial tuberculosis terminated in a miliary spread. When the infection is blood-borne it usually occurs before the condition can undergo further development.

(3) *Spread by the Lymphatics.*—This is undoubtedly the commonest mode. Most authors are agreed that a retrograde spread of infection takes place, but there has been some controversy as to the paths along which this occurs. Shore (1929) states that there is a close relationship between those glands receiving lymph drainage from the lungs and those from the heart, and describes a large mass of glandular tissue above the right lung root, the heart draining only into the lower part of this, which he calls the " caval gland of the heart." He further describes two lymph trunks draining the heart : (1) an anterior that drains chiefly the right ventricle and then empties into the medial members of a small group of glands lying in the mid-line of the body just below the left innominate vein ; and (2) a posterior that drains chiefly the left side of the heart and then empties into the caval gland of the heart. In addition to the above Shore describes the presence of small lymphatic glands interpolated between the points of formation and termination of the lymph-collecting trunks ; these are intra-pericardial in most instances.

From the above statements one deduces that the glands at the root of the lungs are the usual origin and source of spread of tuberculosis to the pericardium. The root glands, as we know, may be the first to become involved in cases of chest tuberculosis, and from here the infection may spread to the pericardium without the occurrence of any spread to the lungs. Pulmonary tuberculosis thus plays little part in the development of tuberculous pericarditis.

In corroboration of this we have seen that the root glands were tuberculous in every case in this series. On examination of the autopsy reports we found that the root glands on the right side, i.e. those including the caval gland of the heart, were most commonly involved. Pulmonary tuberculosis was present in six cases. Dr. Strachan states that he has seen the interpolated intra-pericardial lymph glands involved by the tuberculous process in many cases of tuberculous pericarditis.

Myocardial tuberculosis was present in 10 of our cases—in 6 localized to the right auricle, in 3 generalized, and in 1 only chiefly localized to the left auricle. This suggests a lymphatic plexus or anastomosis in the region of the right auricle. In the same way, in most of the cases of tuberculous myocarditis reported by others the right auricle was most commonly involved.

THE CHANGES IN THE PERICARDIUM

These will be described in three stages.

(1) *The Acute Stage.*—The picture in this stage is one of an acute fibrinous pericarditis similar to that found in rheumatic fever. Its real nature may only

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be discovered on microscopical examination. Resolution, such as usually occurs in a rheumatic pericarditis, is rare.

(2) *The Effusion Stage.*—As the condition progresses, the pericardium, especially the parietal layer, becomes thicker, and this is accompanied by the outpouring of an exudate. The effusion is usually large, for example in one case over four pints of fluid. The fluid is most commonly hæmorrhagic in character, but may be straw-coloured or in some cases may consist of a caseous material similar to that found in tuberculous lungs or glands. It is at this stage that the clinical picture most typical of the condition is found.

(3) *The Adherent Stage.*—At .this stage the effusion becomes smaller, thicker, grumous, or caseous. Adhesions develop between the pericardial layers resulting in loculation of the effusion. Loculation accompanied by roughened or shaggy pericardial surfaces probably only occurs in tuberculous pericarditis. Complete obliteration of the sac ultimately takes place as a result of the fluid becoming thicker and organized. At this stage the adhesions that form are usually intra-pericardial. Extra-pericardial adhesions were found in only three of our cases. This fact accounts for the rarity of systolic rib retraction. Adhesive pericarditis may occur primarily from fibroid tuberculosis without the first or second stages.

SUMMARY AND CONCLUSIONS

Pathological Survey.—Tuberculous root glands were present in all our cases. The tuberculous process was localized to the root glands and pericardium in 10 of the cases. In 6 the lungs, pericardium, and root glands were tuberculous. Terminal miliary tuberculosis occurred in 12 ; in 8 following primary root gland and pericardial tuberculosis and in 4 following primary lung, root gland, and pericardial tuberculosis. Pericarditis from a miliary spread was not seen. Pleural effusions were present in 15 cases, being bilateral in most ; 11 had either an acute pleurisy or pleural adhesions. Chronic congestion of the liver was present in most with either fibrous, fatty, or tuberculous changes.

Clinical Survey.—In spite of the short duration of the history, usually between three and six months, we believe the condition is usually insidious in its onset, and that these Bantu patients only began to notice symptoms when they became severe.

A history typical of congestive cardiac failure was generally given, especially in cases of the effusion type. Contrary to the statements of most authors, we found that there was usually complaint of cough. Hæmoptysis was rare, occurring in 5 cases. Abdominal pain, usually localized to the right hypochondrium, was complained of in 17 ; and 11 complained of chest pain, usually localized to the precordium. Œdema of the legs was found in 11, breathlessness in 11, and 11 complained of loss of weight.

The temperature was raised in 22, either a remittent or intermittent fever. The respiratory rate was increased in 20, and the pulse rate in 29 ; in 3 there was a pulsus paradoxus. Auricular fibrillation and extrasystoles were each seen

once.   A febrile chart, rapid pulse, and breathlessness were found chiefly with pericardial effusions.

Most were poorly nourished, and 15 had an emaciated appearance.   Œdema was present in the legs of 12 and in 3 it was generalized.

Cardiac murmurs were only present in 2, and a pericardial rub in 3.   The heart sounds were usually muffled.

Only 9 had signs of pulmonary tuberculosis ; it was of the primary clinical type of Riesman (1901).   Moist sounds at the bases were found commonly.

The liver was enlarged, and usually exquisitely tender, in 12 ; and 8 had ascites.

The effusion stage is, as we have shown, the easiest one in which to make a clinical diagnosis, the enlarged pear-shaped area of cardiac dullness with an obtuse cardio-hepatic angle being the outstanding sign.

Prognosis

The prognosis is bad.   Death usually occurs in one to six months after the onset of symptoms.   The condition, however, is not always fatal, as shown by the fact that people dying of other causes have been found to have a healed tuberculous pericarditis.   We believe that pericardial aspiration and pneumopericardium improve the prognosis as far as the time of survival is concerned.   This belief is substantiated by the fact that in the only cases which left hospital the pericardium had been aspirated; in one case pneumopericardium had been performed in addition.

The cause of death is either cardiac failure or, more commonly, miliary tuberculosis ; this is common in tuberculous pericarditis and may be due to the presence of tubercle bacilli in the fluid and tissues surrounding the heart. The probable mode of entry of these organisms into the blood stream, particularly in cases with intra-pericardial caseation, is by the rupture of a tuberculous follicle into a vein.

Diagnosis

The two main considerations are the diagnosis of pericardial disease and the establishment of its tuberculous nature.

The main points establishing the former are as follows :

  (a) *In the Acute Stage.*—The presence of a pericardial rub.
  (b) *In the Effusion Stage.*—(1) The absence of a visible or palpable apex beat. (2) The enlarged pear-shaped area of cardiac dullness. (3) The presence of Rotch's angle. (4) The typical radiographic picture of pericardial effusion. (5) Pericardial aspiration.
  (c) *In the Adherent Stage.*—(1) Evidence of cardiac incompetence. (2) Evidence of venous engorgement. The condition is most difficult to diagnose at this stage, and systolic retraction of the ribs has been seen only once.

The following are in favour of a pericarditis being tuberculous :

(1) A patient suffering from a chronic wasting disease.

(2) Fever, intermittent or remittent, with frequent inverse manifestations.

(3) Pulmonary tuberculosis or active tubercle elsewhere (almost conclusive).

(4) Congestive cardiac failure, with a febrile chart and bilateral pleural effusions, without organic cardiac murmurs or evidence of hypertensive disease or coronary thrombosis. Also swelling of the face without kidney damage.

(5) Hæmorrhagic pericardial fluid.

(6) Radiography and probably kymography after pneumopericardium, showing the small heart and thickened pericardial wall.

(7) The finding of tubercle bacilli in the pericardial fluid.

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RIGHT VENTRICULAR HYPERTROPHY OF UN-KNOWN ORIGIN: SO-CALLED PULMONARY HYPERTENSION

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The following three cases are reported since they provide an opportunity for further defining the condition that has been termed primary pulmonary arteriosclerosis. It may be difficult to distinguish clinically from cardiac disease secondary to long-standing pulmonary disease. Brenner (1935) states that : " before the diagnosis of primary pulmonary arteriosclerosis is made, all the factors commonly (though perhaps erroneously) thought to cause secondary pulmonary vascular sclerosis must be absent and there must be marked hypertrophy of the right ventricle." He collected 16 cases, verified at autopsy, that satisfied these criteria; but few were fully investigated, particularly in regard to the relative weight of the right and left ventricles, on which the diagnosis ultimately depends. Lewis (1913–14) has shown that estimates of ventricular hypertrophy in the absence of accurate measurements may be fallacious, and has devised a method for determining the relative degree of hypertrophy of the ventricles by careful dissection and separate weighing. His method has been adopted in the present study, and his series of normal ratios of the relative weights of the ventricles have provided the standard by which the degree of right ventricular hypertrophy has been assessed.

Materials and Methods.—The hearts were severed from the parietal pericardium and great vessels and the chambers were freed from clot and then weighed. After preservation in 10 per cent formalin followed by 70 per cent spirit, the ventricles and septum were dissected from the rest of the heart and weighed separately, according to the method of Lewis. The weight of the left ventricle divided by that of the right provided the L/R ratio.

Sections of the lungs were taken, at intervals of one centimeter, from the hilum to the periphery, and stained with hæmatoxylin and eosin and with Weigert's and Van Gieson's stains for elastic and fibrous tissues.

REPORT OF CASE I

A butler, aged 55, was admitted to Guy's Hospital complaining of shortness of breath and cough. His father had died at the age of 70 and had always been

" chesty " ; there was no other family history of heart or lung disease. He had a wife, who was well, but no children.

He was born in India. There was no history of cardiac disease, but for the past few years he had been " chesty and bronchial." Twelve days before admission he complained of shortness of breath and coughing, of swelling of the ankles and abdomen, and of loss of appetite. Four similar attacks previously had improved with rest in bed, but on this occasion rest did not benefit his condition.

On admission, he was very dyspnœic and showed venous pulsation in the neck and marked œdema of the ankles. The temperature was 98° F. and the respirations were 25 a minute. The pulse was 120 and regular in force and rhythm. The blood pressure was 120/72 mm. The chest showed very little respiratory movement and a few râles were heard. The abdomen contained free fluid. Venesection of 300 c.c. was performed and 500 c.c. of clear fluid were withdrawn from the abdomen.

He gradually sank into coma and died on the night of admission before he could be more fully investigated.

Autopsy (P.M. No. 104/1935)

A middle-aged male of medium build and good musculature, showing bilateral œdema of the lower extremities as far as the knees.

Cardiovascular System.—The pericardial sac was distended by an excess of clear yellow fluid and there were " milk patches " over the right ventricle. The heart was greatly enlarged, more of the enlargement being right-sided. The myocardium of the right ventricle was three to four times its normal thickness ; that of the left ventricle and both auricles showed no abnormality. The myocardium was of normal colour and texture throughout. The tricuspid and pulmonary valves were very dilated, measuring respectively 17·3 and 11·6 cm. in circumference ; they were otherwise normal. The mitral and aortic valves showed slight atheroma, but were otherwise normal. The coronary arteries showed slight fatty atheroma in the beginning of their course, without any appreciable alteration in the lumen. The aorta was of moderate elasticity and uniform diameter and showed patchy atheroma, becoming calcified and ulcerated near the bifurcation. The pulmonary artery was normal, apart from dilatation and slight atheroma in streaks in the main branch. The pulmonary arterial tree was dissected as far as the arteries measuring 2 mm. in diameter, but no abnormality was found. The pulmonary veins were normal. There were no developmental abnormalities present in the heart, aorta, or pulmonary artery.

The weight of the heart, *in toto*, free from clot and including the epicardial fat, auricles, and ventricles, was 650 g. The left and right ventricles, excluding the septum, weighed 140 and 165 g. respectively, and the ratio of left to right was 0·84 (normal L/R ratio = 1·79).

Respiratory System.—The larynx, trachea, and bronchi were normal. The pleural cavities were dry and the pleuræ showed bilateral superficial apical scarring, but were otherwise normal. The right and left lungs weighed 750 and 650 g. respectively, and both showed anterior marginal emphysema of moderate degree and congestion at the bases. Otherwise the lungs were normal.

Histology of Lungs.—The alveoli were of normal size and air-containing. An occasional heart failure cell was present, and at the bases the alveolar walls were irregularly thickened by capillary congestion. Acute or chronic inflammatory disease was absent. The arteries, of 1 cm. to 2 mm. in external diameter, showed crescentic thickening of the intima by varying degrees of atheroma ; though the elastic tissue of

the media was conspicuous, it was impossible to be certain that it was increased. The arteries of less than 2 mm. in diameter were devoid of intimal changes and the media appeared normal. No hyaline necrosis of the vessel wall was seen.

Alimentary System.—The only abnormality was in the stomach, which showed a large chronic ulcer measuring 3 × 2 cm. on the lesser curvature, 5 cm. from the pylorus. One litre of clear fluid was present in the peritoneal cavity. The liver weighed 1600 g. and was normal in size and shape and showed venous congestion. The gall bladder, biliary ducts, and pancreas were normal, as was the histology of the liver and pancreas.

Lymphatic System.—The spleen weighed 200 g., and showed a firm, congested pulp. The mesenteric, cervical, and mediastinal lymph glands were normal. On section the spleen was congested and showed hyaline vascular change in the arterioles.

Urinary System.—Each kidney weighed 200 g. and was normal in size and shape with a smooth surface and loose capsule. The cortical parenchyma was of normal width and pattern. The pyramids were congested and firmer than usual in consistency. The pelves, ureters, and bladder and the prostate and testes were normal. On section the glomerular and intertubular capillaries were moderately congested. The arteries and arterioles were normal. The parenchyma appeared normal.

In this case and in the two that follow, both adrenal glands and the thyroid were normal, to naked eye and on section. The central nervous system was not examined in any of the three cases.

REPORT OF CASE 2

A shop assistant, aged 30, was admitted to Guy's Hospital complaining of shortness of breath. His father had died, aged 48, with thrombosis of the legs ; his mother was alive and well. His only sister had died of pulmonary tuberculosis when 19. He was married and had one son.

He had always enjoyed good health, and was examined for insurance two years before admission and passed fit. There was no history of rheumatism.

One year previously he suddenly became aware that he was short of breath on such slight exertion as running across the road, so that he had to stop and proceed slowly. At this time he noticed that he felt unusually tired after his work. A few weeks later, on getting up at night to attend to his young child, he felt dizzy, fell to the ground, and was unconscious for several minutes. He had two further attacks of unconsciousness. In the first, whilst running for a train, he felt dizzy and thought he was going to faint ; he grabbed a railing, but fell down unconscious and was aroused a minute later by someone speaking to him. A third attack occurred six weeks before admission, whilst he was sitting down after having brought some coal upstairs. There were other minor attacks of dizziness, but without loss of consciousness.

For a few months before admission he had had epigastric pain and diarrhœa, and for the last week had vomited all except light foods. For a month he had had an unproductive cough, and had been sleeping badly. He had been under medical care for six weeks, and for a week had been having digitalis, which was stopped two days before entering the hospital.

On admission, he was cyanosed and restless, but dyspnœa was not marked. Venous pulsation was absent in the neck. The temperature was 95° F. and respirations 20 a minute.

On physical examination, the pulse was regular in force and rhythm over

short periods of a minute or so, but for the space of a few beats the rate would suddenly rise from 40–50 to 80–90 a minute. On palpation of the apex, the rate of the heart was found to be constant at 80–90 a minute, a powerful impulse alternating with a weaker one and only the more powerful being transmitted to the pulse. Occasionally for a few beats all impulses at the apex were of equal strength and transmitted to the wrist. The apex beat was just under the nipple in the fifth intercostal space, and the heart was not enlarged to percussion. A systolic murmur was heard at the apex, but no diastolic murmur could be detected. The blood pressure was 125/95 mm. The liver was just palpable and tender. There was no œdema or ascites. The spleen was not palpable. Nothing abnormal was detected in the respiratory or nervous systems.

The day after admission the heart was beating at 80–90 a minute, the impulses being regular and of equal amplitude and all transmitted to the wrist. There was an occasional extrasystole, and at other times several of these in quick succession would precede a temporary return to the cardiac rhythm found on admission. An electrocardiogram taken on this day confirmed pulsus bigeminus and showed right axis deviation, inversion of T_2 and T_3, and a depression of the iso-electric period after the QRS complex, suggestive of the effects of the digitalis therapy.

Early the following morning he was very restless, and on trying to get out of bed felt dizzy and said he lost consciousness. He was dazed and confused for a short time afterwards, but was not dyspnœic, and recovered quickly from this attack. When examined, the rate of both pulse and apex beat was 90 a minute. That evening there was a return to the cardiac rhythm present on admission ; he became restless and more cyanosed and despite oxygen therapy died the same evening, three days after admission.

Autopsy (P.M. No. 53/1938)

A young male of slight build, of good nourishment, with no external abnormalities. There was no subcutaneous œdema.

Cardiovascular System.—The pericardial sac contained a slight excess of clear yellow fluid. The visceral pericardium showed numerous sub-epicardial petechiæ along the course of the coronary vessels, on both the anterior and posterior surfaces. The heart was extremely enlarged and globular in shape, most of the enlargement being due to hypertrophy of the right ventricle. The myocardium of the right side was thicker than that of the left, but was of normal colour and texture throughout. The tricuspid and pulmonary rings measured 16·0 and 10·5 cm. in circumference, and were very dilated, but the valves were otherwise normal. The mitral and aortic rings were 11·5 and 7·5 cm. in circumference and the valves were normal. There were no endocardial abnormalities. The coronary arteries were of equal size and were free from atheroma. The aorta was of normal elasticity and dimensions throughout and free from atheroma. There were no developmental abnormalities and the ductus arteriosus was closed. The pulmonary artery, throughout its branches, as far as the periphery of the lung, was dilated and showed yellow fatty atheroma in streaks and plaques. The wall was not appreciably thickened, though its branches throughout both lungs were more prominent than normal and slightly rigid. The pulmonary veins were normal. The venæ cavæ and hepatic veins were dilated, otherwise normal.

The weight of the heart *in toto* was 530 g. The right and left ventricles, excluding the septum, weighed 153 and 133 g. respectively, and the ratio of left to right was 0·87.

The histology of the heart was normal.

Respiratory System.—The larynx, trachea, and bronchi were normal. The pleural cavities each contained a few c.c. of clear fluid and the pleural membranes were normal throughout except for very superficial bilateral apical scarring. The right and left lungs weighed 620 and 540 g. respectively, and were of normal shape and size, homogeneous in colour, air-containing throughout, and of normal consistency. The most conspicuous feature in the lungs was the prominence of the dilated atheromatous pulmonary arteries, which extended as far as the periphery. The tracheo-bronchial lymph glands were slightly pigmented, otherwise normal.

Histology of Lungs.—All the sections taken showed some dilatation of the capillaries, but the alveolar spaces were air-containing and devoid of any abnormality. The larger branches of the pulmonary artery from 1 cm. to 3 mm. in external diameter showed irregular thickening of the intima by atheroma, but the media appeared normal. The arteries of lesser calibre than 3 mm. were devoid of intimal changes, while the media appeared thickened by hypertropy, being 20 per cent of the external diameter ; but since the media in arteries of this size varies from 6 to 32 per cent of the diameter with a mean of 16 per cent (Brenner), it is doubtful whether 20 per cent is indicative of medial hypertrophy.

Alimentary System.—The pharynx and œsophagus were congested. The stomach was greatly distended, the mucous membrane was congested, and the rugæ were thickened, but there was no ulceration or scarring. The rest of the alimentary tract and the peritoneum were normal. The liver weighed 1600 g. and was just enlarged, with a slightly granular capsular surface that was firmer than normal in consistency. The cut surface was uniformly mottled by passive venous congestion, but was otherwise normal. The gall bladder, biliary tract, and pancreas were normal. On section the liver showed dilatation and congestion of the sinusoids and central venules, but the parenchyma appeared normal ; the pancreas was normal.

Lymphatic System.—The spleen weighed 110 g. and was normal, except for some hyaline vascular change on section.

Urinary System.—Each kidney weighed 110 g. and was of normal size and shape, with smooth surface and loose capsule. The parenchyma was of normal colour, width, pattern, and consistency. The pelves, ureters, bladder, prostate, and testes were normal. On section the kidneys were congested, but otherwise normal.

REPORT OF CASE 3

A leather dresser, aged 49, was first admitted to Guy's Hospital in February, 1937, complaining of shortness of breath.

Dyspnœa had first been observed by the patient after an attack of influenza in December, 1936. It became rapidly worse, and soon he was unable to hurry even a few yards to catch a bus. At the same time he began to complain of constant precordial pain, uninfluenced by exertion or by the taking of food, but aggravated by deep breathing. For many years he had had a chronic productive cough, which had increased since the onset of his illness. He had never coughed up blood. Apart from this cough, he had always enjoyed good health.

On admission he was orthopnœic and deeply cyanosed. Clubbing of the fingers and toes was present. The pulse rate was about 100 per minute, and the respiration rate varied between 30 and 50 per minute. The temperature was normal. There was no œdema and the venous pressure was not increased. The heart was clinically and radiologically slightly enlarged, but presented no other abnormality. The blood pressure was 104/74 mm. Movement of the chest was poor, and air entry diminished, particularly at the bases, where

rhonchi were present. The liver was just palpable and somewhat tender. No other abnormality was apparent on clinical examination.

Examination of the blood showed a hæmoglobin percentage of 125, 6,600,000 red cells per c.mm., and 9300 white cells per c.mm. All the cells appeared normal. The erythrocyte sedimentation rate was 2 mm. in the first hour. Examination of the urine showed no abnormality. The blood Wassermann and Kahn reactions were negative. Radiography of the chest revealed (erroneously, as was subsequently shown) paradoxical movement of the right hemi-diaphragm, and because of this finding a diagnosis of paralysis of the right phrenic nerve, due to carcinoma of the bronchus, was made.

However, by March he was able to return home and gradually got well enough to resume his work in April. He remained well, putting on a good deal of weight, until November, when his dyspnœa suddenly returned and became rapidly worse.

He was then re-admitted to Guy's Hospital, the clinical features being substantially the same as before, though the cyanosis and dyspnœa were not so prominent. Electrocardiography showed marked right axis deviation, with low voltage, and flattening of T_3. An X-ray of the chest showed slight widening of the mediastinum and some enlargement of the pulmonary artery. The previous finding of paradoxical movement of the right hemi-diaphragm was confirmed during normal breathing, but on deep inspiration normal movement took place.

The diagnosis was considered to lie between " Ayerza's disease " and carcinoma of the bronchus. In view of the latter possibility a course of deep X-ray therapy was given, after which the patient was discharged in January 1938.

He remained well and at work for several months until February, 1939, when the dyspnœa returned and rapidly grew incapacitating. He was re-admitted in March in a very distressed state, with marked orthopnœa and severe cyanosis, but without venous engorgement and with only very slight œdema of the ankles. There was no pyrexia and the pulse rate was regular at about 100 per minute. Respirations varied between 30 and 60 per minute. The blood pressure was 120/72 mm. The apex beat could be felt five and a half inches from the mid-line in the fifth intercostal space, and no abnormality was apparent on auscultation of the heart. Movement of the chest was slight, but apart from widespread rhonchi no clinical abnormality was present. The liver was not palpable. Examination of the urine showed no abnormality.

An X-ray of the chest revealed enlargement of the heart (transverse diameter 17 cm. in a chest of 28 cm.). The pulmonary artery and conus of the right ventricle were very prominent. The pulmonary arterial tree was well marked, but apart from this the lung fields were normal. An electrocardiogram showed very little change from that of a year before. Blood circulation times were also measured, the arm-to-lung time (paraldehyde) being 10 seconds and the arm-to-tongue time (decholin) 15 seconds ; these figures lie within the normal range.

On the diagnostic grounds enumerated below, the case was considered to

be one of primary pulmonary hypertension. Treatment was carried out in the oxygen tent. During the next few weeks the clinical condition fluctuated considerably, but some degree of dyspnœa and cyanosis was always present. Death occurred suddenly after four weeks in hospital.

Autopsy (P.M. No. 138/1939)

An elderly obese male of hypersthenic build, with barrel-shaped chest and wide intercostal angle. The fingers were clubbed and the ankles slightly œdematous.

Cardiovascular System.—The pericardium was slightly adherent to the right pleura by a few delicate fibrous bands. The sac and contents were normal except for a " milk patch " on the anterior surface of the right ventricle and a few petechiæ along the coronary sinus. The heart was globular in shape and much enlarged, due to great hypertrophy of the right ventricle. The myocardium of the right ventricle was two to three times the normal thickness, with hypertrophied columnæ carneæ and papillary muscles. That of the left ventricle and auricles was normal. The myocardium was of uniform colour, texture, and consistency. All the chambers were dilated and filled with post-mortem clot. The tricuspid and pulmonary rings were dilated and measured 13·5 and 10 cm. in circumference, but the cusps were normal. The mitral and aortic rings were 11 and 7·5 cm. and both valves were normal, apart from fatty atheroma of the anterior cusp of the former. The coronary arteries were of equal size and showed slight fatty atheroma at the beginning, but their lumina were not narrowed and were normal and patent throughout. The aorta was of normal elasticity and width, and showed a few patches of atheroma in the sinus of Valsalva, in the arch, and in the abdominal portions only. The pulmonary artery was uniformly dilated as far as the first division. The second branches of the pulmonary artery were more conspicuous than normal and showed patches of fatty atheroma. The remaining branches as far as those of 2 to 4 mm. diameter appeared normal. There were no developmental abnormalities in the heart or great vessels.

The heart weighed 630 g. The right and left ventricles, excluding the septum, weighed 162 and 129 g. and the L/R ratio was 0·80.

Respiratory System.—The larynx, trachea, and bronchi contained frothy mucus and the mucous membrane was congested and slightly granular and covered by a delicate fibrinous exudate. The left pleural cavity was dry and the pleura was normal throughout. The right pleural cavity was obliterated over the upper lobe and showed a few basal pleuro-pericardial fibrous adhesions. Elsewhere it was normal. The right and left lungs weighed 1000 and 800 g. respectively and were of normal size and shape. There was slight bullous emphysema along the anterior margins of both upper lobes, and the remainder of the lungs was slightly congested and œdematous, but of normal consistency and air-containing throughout. The bronchi were of normal diameter and, apart from slight congestion of the mucous membrane, were normal and free from inflammatory exudate. There was no evidence of acute or chronic inflammation in either lung. The tracheo-bronchial lymph glands were pigmented, but otherwise normal.

Histology of the Lungs.—The capillaries throughout the lung were engorged and the alveoli air-containing and devoid of cells. No abnormality could be detected in the arteries of 1 cm. to 0·2 cm. in diameter. In some sections the smaller arteries were dilated; in others they appeared constricted. There was no inflammatory disease.

Alimentary System.—No abnormality was detected. The liver weighed 2100 g. and was enlarged, with smooth surface and rounded edges. The cut surface was uniformly pale, with slight accentuation of the normal lobularity, and on section showed dilatation of the sinusoids. The gall bladder contained 50 c.c. of concentrated bile, which flowed freely, and the mucous membrane contained cholesterol deposits. The biliary passages and pancreas were normal.

Lymphatic System.—The spleen weighed 300 g. and was enlarged, with smooth capsule and a firm, uniformly congested pulp ; on section it showed hyaline vascular change only. The cervical, mediastinal, mesenteric, and inguinal lymph glands were normal.

Urinary System.—The right and left kidneys weighed 220 and 210 g. respectively, and were enlarged but of normal shape. The surfaces were smooth, with loose capsules. The cortices were of normal width and the vascular pattern was accentuated. The boundary zones were sharply defined and the pyramids deeply congested. The parenchyma was firmer than normal. The pelves, ureters, and bladder were normal, as were the prostate and testes. On section the kidneys were slightly congested, but were otherwise normal.

CLINICAL CONSIDERATIONS

From the study of these cases and those previously reported the chief points in the diagnosis of primary pulmonary hypertension would appear to be as follows :

1. There is central cyanosis, with which may be associated polycythæmia and clubbed fingers.
2. Dyspnœa may be the presenting symptom, but does not become extreme.
3. There is hypertrophy of the right ventricle, which sometimes may be demonstrable only by X-ray examination.
4. Radiological evidence of dilatation of the pulmonary artery and of the right ventricular conus is present. This is probably the most important clinical finding, as it is not present to the same degree in heart failure secondary to lung disease.
5. There is no clinical, radiological, or pathological evidence of serious disease of the lung parenchyma.
6. The second pulmonary sound may be accentuated, but otherwise no signs of organic heart disease are present.
7. Electrocardiography shows right axis deviation and flattening or inversion of the T waves in leads II and III.
8. Increase of the systemic venous pressure and œdema occur only in the late stages when the heart fails.
9. The systemic arterial blood pressure is not increased.
10. There is no evidence of syphilis.

The distinction between pulmonary hypertension and cardiac failure secondary to chronic lung disease may not always be easy to make, especially where there is a history of dyspnœa. But X-ray and electrocardiographic evidence of marked right-sided cardiac hypertrophy or preponderance is not commonly found as a result of emphysema (Parkinson & Hoyle, 1937). On clinical evidence the first case might be regarded as one of " cor pulmonale," since the patient had been described as " bronchial and chesty " for some years before the onset of symptoms suggestive of cardiac failure. The slight changes found in the bronchi and lung parenchyma post-mortem, however, did not appear to be sufficient to account for the marked hypertrophy of the right heart and dilatation of the pulmonary artery. The third case was said to show clinical emphysema, but in view of the difficulty in diagnosing emphysema at

the bedside and the slight extent of the emphysema at autopsy we feel that this clinical finding may be dismissed.

A clinical diagnosis of Ayerza's disease is sometimes made in this type of case, but as there is no generally accepted definition of what is meant by this term it is better avoided. Congenital heart disease or mitral stenosis may cause difficulty in diagnosis. In the absence of the usual signs of these conditions, excessive cardiac pulsation or the smallness of the aorta may be of importance in distinguishing congenital disease, and the marked vascular changes at the hila and enlargement of the left auricle in distinguishing mitral stenosis.

The disease appears to run a course of from five months to five years after the onset of symptoms, the average expectation of life being two years. Our patients survived twelve days, twelve months, and twenty-eight months after the onset of symptoms. No specific treatment for the condition has been suggested ; oxygen therapy appeared to benefit the third case, but such treatment can only be symptomatic.

It might be presumed that the second patient, a man of 30 years, would demonstrate the features of the disease in a clearer manner than the other two cases, in which arteriosclerosis might have been a complicating factor. This patient may be compared with the first case of Brenner, a boy of 11 years. The first symptom noticed by both was dyspnœa on exertion. Both were markedly cyanosed, and suffered from attacks of unconsciousness. It is probable that the condition produces no symptoms until the enlarged right ventricle begins to fail, but in some respects the early symptoms appear to differ from those usually seen in right heart failure. The dyspnœa observed in the early stages does not appear to progress with the course of the disease, and the presence of marked cyanosis with the absence of systemic venous engorgement is remarkable. The cyanosis is due to the inadequate oxygenation of the blood in the lungs, but the reason for this is obscure. The rate of blood flow through the lungs, as judged by the measurement of the circulation times, appears to be unaltered, and there is no evidence of vascular congestion in the lungs. Moreover, histological study of the lung fails to reveal any change in the alveolar wall which might impede the passage of oxygen through it. The diminished oxygen content of the arterial blood is probably a more important factor in the causation of the dyspnœa on exertion than the possible presence of circulatory failure. Since the ventilating powers of the lungs are inadequate even at rest, it is suggested that they would prove even more so with the increased demand of the body for oxygen during exertion. A further lowering of the arterial oxygen content would also explain the syncopal attacks, which in their clinical features may be compared to Stokes-Adams seizures, and may be regarded as evidence of cerebral anoxia.

PATHOLOGICAL FINDINGS

The only anatomical feature that was striking and common to all three cases was the great hypertrophy of the right ventricle, indicated by the L/R ratios

of 0·84, 0·87, and 0·80.   The normal ratio given by Lewis (1913–14) is 1·79, while that for eight cases of uncomplicated mitral stenosis was 1·0, showing that the relative degree of right ventricular hypertrophy in the present condition exceeds that found even in mitral stenosis.

The degree of atheroma of the pulmonary arterial tree varied, being conspicuous in the second, moderate in the third, and slight in the first case, and bore no relationship to the degree of ventricular hypertrophy.   There was no clinical evidence of systemic hypertension, and the slightness of the left ventricular hypertrophy and the pathognomic sign of hyaline or " fibrinoid " necrosis in the intralobular arteries and afferent arterioles of the kidney is also against the co-existence of systemic hypertension (Hadfield and Garrod, 1932).

The histological changes in the pulmonary blood vessels, apart from intimal atheroma, were insignificant.   There was no intimal thickening, medial hypertrophy, or any of the changes that are found in the small arteries and arterioles of the systemic circulation when systemic hypertension is present.   In this connection it may be pointed out that such changes occur mainly in the smaller muscular type of arteriole, which is absent in the lung, where even the smaller arteries down to 0·1 mm. diameter are of the elastic type with a relatively thin media.   There are no vessels in the pulmonary arterial tree comparable to the afferent arteriole in the kidney, and the absence of a susceptible vessel may be a possible explanation for the lack of such lesions in the present cases.   The diameter of the arterial lumen and the ratio of the lumen to the vessel wall varied too much to be of any significance.   In the first case there was no appreciable difference from the normal; in the second the arteries down to less than 0·1 mm. in diameter were uniformly dilated; whereas in the third the degree of contraction varied in different sections.   In fact, there were no structural changes that could be considered abnormal.   Similarly, the parenchyma of the lung was devoid of any evident abnormality.

PATHOGENESIS

With regard to the ætiology and pathogenesis of the condition, there is little to add to Brenner's statement : " In most cases the changes appeared to be those of ordinary atherosclerosis and to be non-inflammatory.   Most authors have suggested that primary sclerosis is caused by pulmonary vascular hypertension either due to spasm of the pulmonary arterioles or to congenital narrowness of the pulmonary veins.   There is no evidence in favour of either of these suggestions and the cause remains unknown."   Since Brenner's articles, further cases of primary pulmonary arteriosclerosis have been published.   Kaump and Dry (1938) reported one, in which no adequate reason for the hypertrophy of the right ventricle could be found, and Rothschild and Goldbloom (1938) recorded a case of " obliterating pulmonary arteritis " and right ventricular hypertrophy and considered that the condition was allergic, but in the absence of heart weights it is impossible to assess their significance.   Seely (1938) reported a case of primary obliterative pulmonary sclerosis in which the heart weighed 390 g. against a normal average of 303 g. for a female of 68 (Bell and

Hartzell, 1923–4) ; the lungs weighed 200 and 170 g. and were emphysematous. In view of the possibility, so far not proven, that emphysema may cause right ventricular hypertrophy, it is possible that the hypertrophy in this case was secondary to the emphysema. Alexander *et al.* (1927) in a clinical study of 50 patients with true bronchial asthma, evident for at least five consecutive years and of an average duration of ten years, found that emphysema was present in all except one. Examination of the heart revealed three patients with " cardiac injury," and in two of these the cardiac lesion antedated the asthma. In view of the difficulty of estimating the degree of emphysema both clinically and pathologically, the relationship between it and right ventricular hypertrophy is still a matter for conjecture. Parkinson and Hoyle found that great enlargement of the right heart is rare in emphysema, having been seen in only four cases out of eighty ; they conclude that the cardiac symptoms and signs in emphysema are more likely to be due to an accompanying systemic hypertension than to the direct effect of emphysema on the heart. There is no experimental evidence to show that any diminution in the pulmonary capillary bed, such as might occur in emphysema, causes an increase in blood pressure in the right side of the heart. Dunn (1919) occluded large areas of pulmonary circulation by injection of starch or oil in the jugular veins of animals and showed there was no alteration of blood flow through the lungs or in the pressure in the right side of the heart.

The most conspicuous anatomical abnormality in the pulmonary circulation of these cases is the great hypertrophy of the right ventricle. Does this single anatomical fact justify the opinion that the hypertrophy is a physiological reaction to increased work, and is therefore analogous to the left ventricular hypertrophy in systemic hypertension ? Whereas in the latter the ventricular hypertrophy is associated with characteristic lesions in the systemic arteries and arterioles, but is independent of the degree of arteriosclerosis, right ventricular hypertrophy is unassociated with any such comparable lesions in the smaller pulmonary arteries. An explanation of the lack of arteriolar changes may be that such changes in the systemic arteries are usually confined to the muscular type of artery, which is absent in the pulmonary circulation. The existence, therefore, of pulmonary hypertension is conjectural, and is not justified on analogy alone. If a name based on the morbid anatomy is required for this condition, " idiopathic right ventricular hypertrophy " would appear to be a suitable one, until such time as the condition may have acquired a proved ætiology. The term " pulmonary arteriosclerosis " is misleading, as the arteriosclerosis would seem inadequate to account for the ventricular hypertrophy.

SUMMARY

1. Three cases of severe right ventricular hypertrophy of unknown origin have been described.

2. The usually accepted causes of such hypertrophy due to disease of the heart and lungs have been excluded.

3. The clinical and pathological changes have been described and discussed.

4. It is suggested that the term " idiopathic right ventricular hypertrophy " should in future replace " primary pulmonary arteriosclerosis " or " hypertension," which have no foundation in fact.

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PULMONARY HYPERTENSION

BY

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This title has been chosen deliberately, although it denotes something hypothetical, as indicating a possible cause of the facts hereafter described.

These three cases were reported at the meeting of the Cardiac Society at Birmingham in 1939. The subsequent outbreak of war has made it impossible to survey the literature, so there are no references. I think, however, that the accurate presentation of the observations is the important thing. There can be no doubt that we are confronted with a curious and hitherto rare condition ; its nature and causation will need further study, but the account of these three cases may be helpful and may draw attention to others.

NOTES OF FIRST CASE

A married woman of 31, with one child aged 6, was first seen in December 1936, complaining of dyspnœa even on walking on the level. She also noticed palpitation, and had to sleep supported by three pillows, though there had been no dyspnœa at night. These symptoms had been coming on gradually for two or three years. There was no history of rheumatic fever or any important illness.

She was of medium build, with a flattish chest and a somewhat depressed lower end of the sternum. The lips were slightly cyanosed. There was no œdema, and the liver and external jugular veins were not engorged. The heart was enlarged (15 cm. in transverse diameter on screening). The electrocardiogram in this case (Fig. 1A), as in the others, indicated that the increase in size was in the right ventricle. Clinically, enlargement was obvious in the region of the pulmonary artery and conus arteriosus. Here one could detect definite systolic pulsation, a slight systolic murmur, a very loud pulmonary second sound, and an easily palpable closure of the pulmonary valves. Screening showed the greatly enlarged pulmonary artery (Fig. 2A) and its branches seemed conspicuous, for there was a definite " hilar dance." The lungs were clear. The left auricle was not enlarged (Fig. 2B). The peripheral arteries were normal. There was slight polycythæmia ; red cells 6·4 million, hæmoglobin 126 per cent. There was no clubbing of the fingers. The Wassermann reaction was negative. B.P. 125/70. The enlargement of the right ventricle and of the pulmonary artery and its branches prompted ·a diagnosis of patent interauricular septum.

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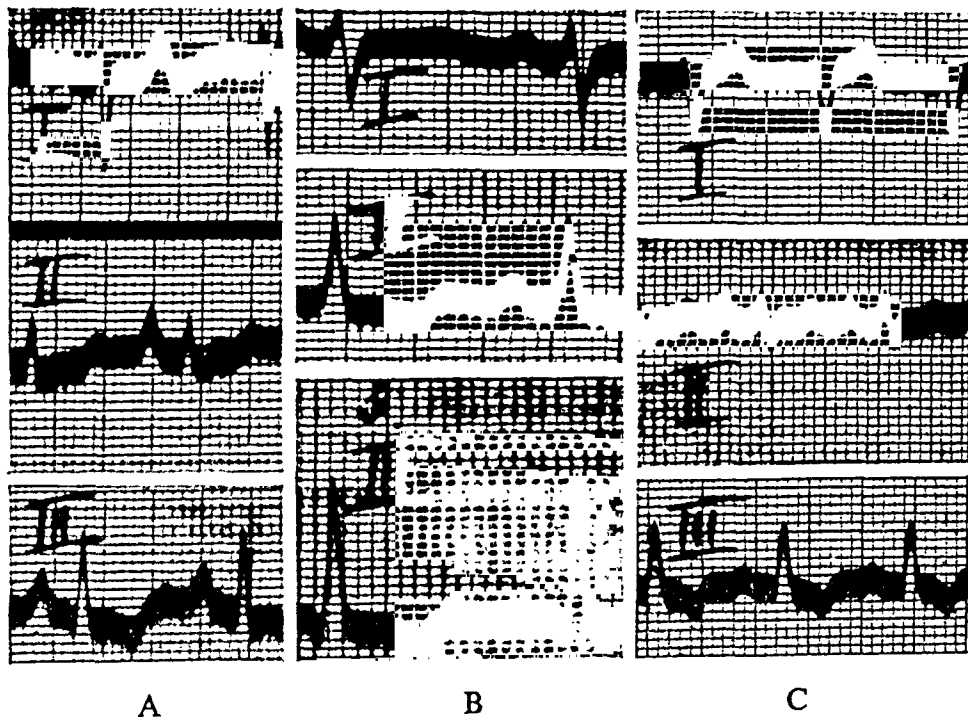
Fɪɢ. 1.—Electrocardiograms showing right axis deviation.   (A) Case 1, five months before
death ;   (B) Case 2 ;   and (C) Case 3.

Fɪɢ. 2.—Case 1.   (A) Antero-posterior view, five months before death. Note the large
pulmonary artery.
(B) Right anterior oblique view.   Note the normal left auricle.

Clinical Course

In the next month signs of congestive failure of the right ventricle came on, with great enlargement of the liver, ascites, venous engorgement, and increasing cyanosis and œdema. The heart rate remained regular and between 60 and 90, and the respiratory rate did not rise above 20. In the last week the heart rate rose to 120, with regular rhythm ; she became more cyanosed and drowsy, and finally died quietly without distress in May 1937.

Post-Mortem Findings

In this case the ventricles were weighed separately, after being dissected from the auricles and divided down the middle of the septum.

Heart.—Right auricle much dilated and full of post-mortem clot. Foramen ovale closed. Tricuspid valve flaps normal ; valve enlarged, admitting four fingers, the circumference being 14 cm. Right ventricle greatly enlarged (195 g.) with huge increase in capacity, and massive musculature of the trabeculæ ; the apex actually formed the apex of the heart. Wall 5 mm. thick, two cm. from the apex. Interventricular septum closed. Pulmonary artery large and prominent, and valves capacious and competent, the internal circumference at the top of the cusps being 90 mm. No atheroma in pulmonary artery or its branches and no macroscopic abnormality in smaller twigs. Left auricle small with normal thickness of wall ; mitral valve admitted three fingers, the circumference of the ring being 10 cm. ; slight thickening of the anterior cusp. Left ventricle of normal size, weighing when separated 135 g. ; thickness of the wall, two cm. from the apex, 7·0 mm.

Myocardium throughout looked healthy, with good colour and resilience ; microscopical sections showed fibres of the right ventricle hypertrophied. Coronary arteries, normal.

Lungs.—These were a little collapsed at the bases from upward pressure by the abdomen distended by ascites. There was no emphysema or brown induration and they were remarkably free from œdema and engorgement ; no sections were made of the lungs. Elsewhere, the usual changes due to severe and long-standing venous engorgement.

Summary

In this case the outstanding finding was the gross hypertrophy of the right ventricle and enlargement of the pulmonary artery, for which no cause was apparent to the naked eye. The state of the lungs and of the left auricle would exclude any cause affecting them from the left side. The findings confirmed the clinical observations, but not the suggested cause ; nor did they point to another.

NOTES OF SECOND CASE

A married woman of 24, pale and without cyanosis, seen in the autumn of 1938; she gave a history of several attacks of right ventricular failure in the last six years. During the last year she had been more or less an invalid and three

months ago her abdomen had twice been tapped for ascites. She said she had never had rheumatism. The feet were slightly swollen. The liver was enlarged and soft and a little tender. The external jugular veins were not distended, but filled on pressing on the abdomen.

Clinically, the right ventricle was much enlarged. This was confirmed by the cardiogram (Fig. 1B) and by the skiagram (Fig. 3). There was systolic

Fig. 3.—Case 2. Antero-posterior view, three weeks before death. Note large pulmonary artery.
    The right anterior oblique view, with barium in the œsophagus to show the absence of enlargement of the left auricle, has been superimposed in the space between the right border of the heart and the right chest wall.

pulsation in the pulmonary area, with palpable closure of the pulmonary valves and a very loud pulmonary second sound. The left auricle was normal in the oblique view (Fig. 3). There was a slight local systolic murmur at the apex.

Respiration was easy and quiet at 20 per minute, and the lungs were clear. The heart rhythm was regular, with a rate of 90. B.P. 118/78. Slight albuminuria.

Clinical Course

Under treatment she improved so much that she was ready to go home. The day before, she suddenly became drowsy and the abdomen filled up ; the next day she was collapsed, pale, and cyanosed, with transient auricular fibrillation ; a few crepitations appeared at the bases, the pulse became imperceptible, with but little increase in the rate of respiration ; and in a few hours she was dead.

Post-Mortem Findings

Heart.—Slight increase of fluid in the pericardial sac. Total weight 425 g. Right auricle much distended. Right ventricle very large (210 g.) with massive walls and thick trabeculæ. Tricuspid valve, normal flaps, with large orifice, admitting four to five fingers. Pulmonary valves large and competent ; pulmonary artery large, with internal circumference just above the cusps of 90 mm. Several small oval atheromatous patches, 3–5 mm. long, near the bifurcation, with smaller ones in the first main branches. Left auricle normal in capacity and thickness of walls.

Mitral valve, slight thickening of posterior cusp due to old rheumatic carditis ; orifice admitting two fingers. Left ventricle small, with normal walls (weight 131 g.). Coronary arteries normal. Myocardium rather pale, but resilient. Ductus closed and septa whole. Aorta and aortic valves normal. Aorta 70 mm. in internal circumference at the valves.

Lungs.—L., 375 g. ; R., 415 g. A little œdema of the right upper lobe and some congestion of the right lower lobe. Bronchioles rather red, with a little muco-pus. On the whole, very free from congestion and œdema, and without brown induration.

There were the usual changes due to chronic congestion in the liver, kidneys, and spleen, with much ascites and some œdema.

Microscopical Findings

Section of the myocardium showed hypertrophy of the fibres of the right ventricle (Fig. 4). The lungs showed some catarrhal cells in the alveoli. The muscle coats of the arterioles were perhaps a little hypertrophied (Fig. 5). There was no proliferation of the intima or obliteration of the lumen to be seen.

Summary

In this case again there was, at the end, great hypertrophy of the right ventricle, with enlargement of the pulmonary artery. No structural changes were to be detected as a cause. The clinical course was rather long, with recurrent attacks of failure of the right ventricle. As in the first case, the slight degree of dyspnœa was worth noting. The rhythm remained regular, apart from one short bout of fibrillation, which was probably a result rather than a cause of failure. The final failure was sudden and rapid.

FIG. 4.—Case 2. (A) Section of right ventricle showing hypertrophy ; (B) Section of left ventricle for comparison. Magnification × 180.

FIG. 5.—Case 2. Pulmonary arteriole, showing perhaps some hypertrophy. Magnification × 120.

NOTES OF THIRD CASE

A married woman of 31, who came into hospital early in 1939. During the summer before she had begun to notice undue dyspnœa and distress when playing tennis. There was no history of rheumatism. She had had a miscarriage with a hydatidiform mole five weeks previously. There had been increasing dyspnœa on exertion for some months, becoming much worse since the miscarriage. Œdema of the feet had appeared within the last few days. She had had no cough, nausea, or vomiting.

The hands and feet were cold and blue ; the lips, cheeks, and ears were blue. The legs were œdematous and there was a sacral pad. The liver was a little enlarged, and there was some congestion of the external jugular veins. The lungs were clear and there were no rales ; respiration was easy, without any cough or distress, at 20 to 24 per minute. She could lie flat without discomfort ; and was rather quiet and apathetic.

The heart showed an increase of the right ventricular thrust, with systolic pulsation in the pulmonary area. The closure of the pulmonary valves was palpable, and the pulmonary second sound was very loud. Gallop rhythm was audible near the left edge of the sternum. There were no murmurs. The pulse was regular and very weak, with a rate of 115. No blood pressure reading could be obtained. The urine contained much albumen. The blood urea was 90 mg. per c.c. The cardiogram confirmed the gross enlargement of the right ventricle (Fig. 1C). A skiagram (Fig. 6) showed the great heart shadow, with prominence of the pulmonary artery.

FIG. 6.—Case 3. Antrro-posterior radiogram, 24 hours before death. (Taken in bed.)

Clinical Course

During the next twenty-four hours she rapidly became worse. Drowsiness came on and she tended to slip down ; in fact, she lay flat with no inconvenience or dyspnœa ; the breathing was regular and the rate did not rise above 24 until just before the end. The cyanosis increased, and the jugular veins became more distended. Venesection was ineffectual, for only an ounce or two of very thick,

dark blood could be obtained. The heart rate increased to 140, with regular rhythm ; drowsiness increased to coma, and she died in a few hours.

I would comment now upon the clinical picture of pure right ventricular failure. Usually one sees it secondary to failure of the left side, or the case is one of mitral disease with embarrassment of the pulmonary circulation ; or there is pulmonary disease, such as emphysema or bronchitis. Here, all the points were clear and uncomplicated. One was struck by the absence of dyspnœa. The veins filled up, the liver became more engorged, and the cyanosis increased, but the pulmonary circulation remained free from difficulties, so that the breathing continued easy until the patient was nearly dead. It is rare in my experience to witness such a pure and rapidly progressive failure of the right ventricle. What one saw bore out fully the modern theory that cardiac dyspnœa is the result of engorgement of the pulmonary circulation.

Post-Mortem Findings

A well-nourished woman, with œdema of the legs, chest, and abdominal wall, and with intense cyanosis of face, ears, and fingers.

Heart.—Weight 372 g. Right auricle and great veins very engorged. Tricuspid valve enlarged, taking four fingers. Right ventricle very capacious, with massive hypertrophy of its walls, and huge trabeculæ (weight 180 g.) : muscle firm and resilient and of good colour. Pulmonary valves large and competent. Pulmonary artery large, with an internal circumference just above the cusps of 85 mm. (normal, about 66·5 mm.) ; slight atheroma in small flecks and spots. Left auricle of normal capacity and thickness, mitral valve taking two fingers ; very slight thickening at the edge of the cusps. Left ventricle of normal size and capacity (weight 112 g.) Aortic valves normal ; also aorta, coronary arteries, cardiac septa, and ductus arteriosus.

Lungs.—Right lung 465 g. (15 oz.). Slight collapse at extreme base posteriorly. No œdema, engorgement, or induration. A little muco-pus in the bronchioles. Right pleural sac, 300 c.c. clear fluid.

Left lung, 445 g. (14 oz.) ; slight œdema at the extreme base ; no induration or engorgement. Both lungs were, in fact, remarkably light and dry and free from engorgement or œdema.

The liver showed pronounced nutmeg changes ; there was some ascites and congestion of the spleen. The kidneys were rather small, with slight patchy scarring, scattered irregularly on the surface, and affecting the cortex but little underneath it.

Microscopical Findings

The fibres of the right ventricle were hypertrophied (Fig. 7), but no disease of the myocardium was found. In the *lungs* the tissue itself was free from disease. The muscular coats of the smaller arterioles were perhaps a little thickened. Here and there a few of the smallest arterioles were partly obliterated by proliferation of the intima, but this was not a common finding (Fig. 8A).

A few of the larger arterioles showed crescentic patches of intimal proliferation, with some vacuolar degeneration (Fig. 8B).
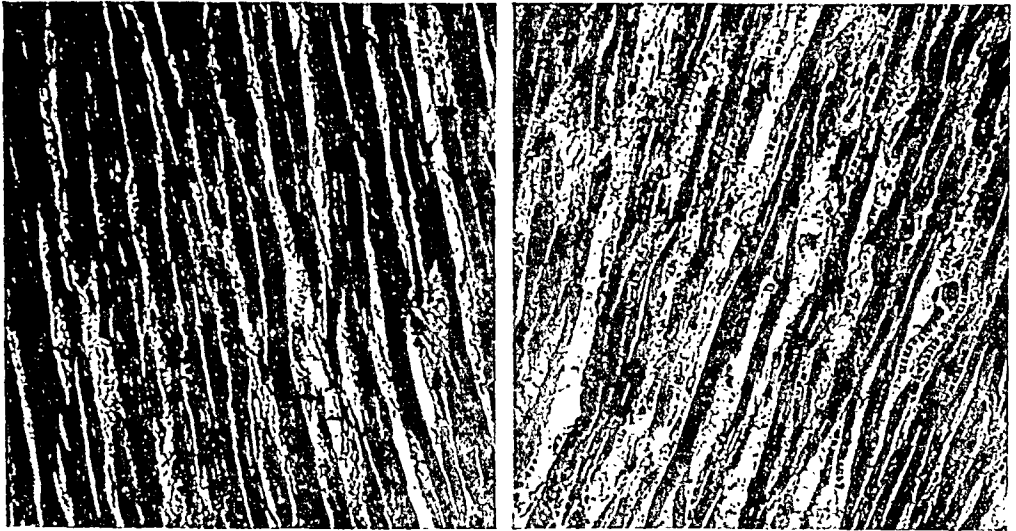
A   B

FIG. 7.—Case 3. (A) Section of right ventricle showing hypertrophy ; and (B) section of left ventricle for comparison. Magnification × 180.
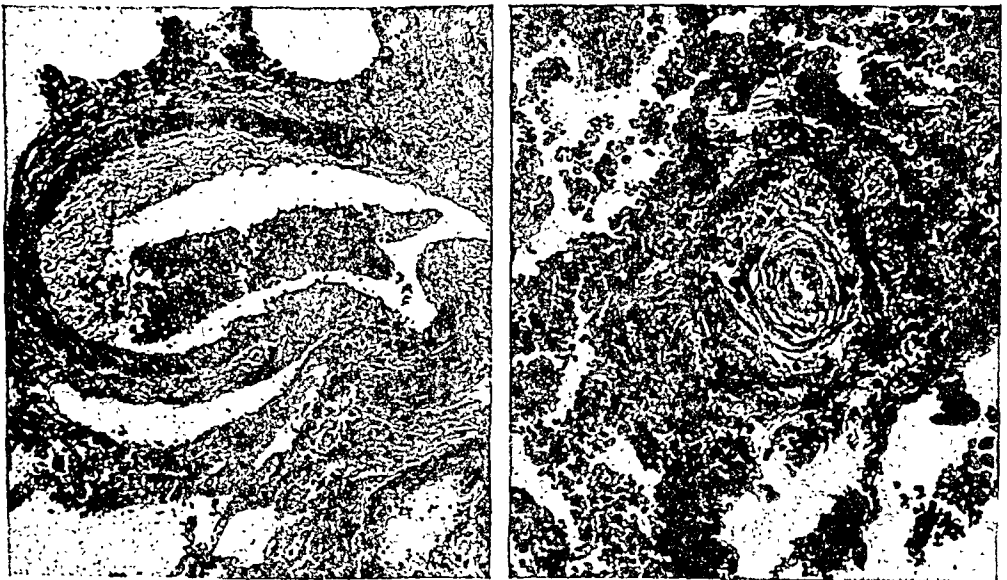
A   B

FIG. 8.—Case 3. Arteriole in lung. (A) Magnification × 100; and (B) Magnification × 200.

Summary

This patient died of pure right ventricular failure which progressed rapidly towards the end. The autopsy showed great hypertrophy of the right ventricle,

and some increase in the size of the pulmonary artery. Some pulmonary arterioles showed an obliterative process. The lungs were free from disease, congestion, or œdema.

SUMMARY OF AUTOPSY FINDINGS

This is a summary of certain measurements of the hearts of these three cases. The normal figures are taken from Vierordt's well-known " Tabellen " for persons of similar age and sex.

TABLE I

WEIGHT OF THE RIGHT AND LEFT VENTRICLES

	Weight in Grammes			
	Normal (Vierordt)	Case 1	Case 2	Case 3
Heart	250	415	391	372
Right Ventricle (separated from Lt.) ..	59	195	210	180
Left Ventricle (separated from Rt.) ..	120	135	101	112
Auricles	85	85	80	80
Lungs : Right	500	—	415	465
Left	425	—	375	445

The great increase in the weight of the heart was due to the increase in the bulk of their right ventricles : whereas the left ventricle is about twice the weight of the right, here in one case the right ventricle was twice the weight of the left ; in the others it was 50 per cent heavier.

The photomicrographs and cardiograms agreed with the diagnosis of hypertrophy.

The weights of the lungs confirmed their normal appearance and the absence of œdema or engorgement.

Table II shows the measurements of the internal circumference of the pulmonary arteries and aortas of these cases, taken just above the valves, and compared with Vierordt's normals :

TABLE II

A COMPARISON OF THE SIZE OF THE AORTA AND OF THE PULMONARY ARTERY IN THESE CASES AND IN NORMALS

	Internal Circumference in Millimetres			
	Normal (Vierordt)	Case 1	Case 2	Case 3
Aorta	55–79 (range)	68	70	60
Pulmonary artery	66·5 (average)	90	90	85

These measurements after death confirm the suggestion of enlargement of the pulmonary artery which one gained during life, clinically and by the skiagram.

DISCUSSION

It remains to produce some explanation for the findings in these three young women. I think that the cases are similar : the age and the clinical course in each case are much alike. To explain pure failure of a greatly hypertrophied ventricle is the problem.

The enlargement of the pulmonary artery must be explained. It might be caused by increase of the blood entering it, as in thyrotoxicosis or as in the patent septa or patent ductus arteriosus ; but those defects were wanting. Increase in the pressure above the valves would also cause it, as in severe mitral stenosis or in some cases of emphysema or with extensive obliteration of the pulmonary arteriolar bed.

The slight thickening of the mitral flaps can have had no effect on the right ventricle ; particularly with the normal appearance of the left auricles before and after death.

There was no disease of the lung tissues.

In one case the pulmonary arterioles showed some degree of obliteration here and there, but it is hard to believe this was extensive enough to affect the right ventricle. The other case showed no change in the pulmonary vessels, but the right ventricle was just as large. Of the third the lungs were not sectioned. The flecks of atheroma were such as one sees often enough in the pulmonary artery in mitral stenosis or in some cases of emphysema when the tension in the artery has been high ; but it may be found when no increase in tension may be supposed to have existed. It seems possible that the changes, atheromatous and obliterative, found in the pulmonary arteries and arterioles in those cases may be the result of high pressure in the pulmonary circuit.

SUMMARY

Three cases are described in which failure of a conspicuously hypertrophied right ventricle took place. At *autopsy* no satisfactory cause for this hypertrophy could be found.

They present a *clinical picture* which should be fairly easily recognizable during life.

1. Enlargement of the right ventricle, with the characteristic electrocardiogram.
2. Enlargement of the pulmonary artery, confirmed by the skiagram.
3. A loud pulmonary second sound suggesting a high pressure in it.
4. Intractable and progressive failure of the right ventricle, with the maintenance of normal rhythm, dyspnœa of any severity being absent.
5. A normal appearance of the left auricle.

6. An absence of valvular defects, congenital or acquired, or of patent septa.
   (Patent interauricular septum might be difficult to exclude.)
7. An absence of pulmonary disease.
8. The absence of evidence of syphilis.

It is suggested that a condition of idiopathic or essential pulmonary hyper-
tension may exist as a cause for those findings.

FAILURE OF THE RIGHT VENTRICLE

A CASE REPORT

BY

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Within recent years the belief that one ventricle may fail without coincident failure of the other has been steadily gaining ground against the older hypothesis of Mackenzie that the heart must always fail as a whole. Much recent work, in America and elsewhere, recently reviewed by Bedford (1939), has shown that hypertension and aortic valvular lesions can occasion a failure of the left ventricle with little or no failure of the right ventricle. The finding of pulmonary congestion and delay in the arm-to-tongue circulation time in patients showing a dilated failing heart in the absence of a rise of venous pressure is convincing support for this theory.

Although separate failure of the right ventricle is theoretically possible, it has been discussed less and its application to the general problems of cardiology has often been too little emphasized. McGinn and White (1935) and White (1935) have shown that an acute failure of the right heart may be rapidly produced by pulmonary embolism. A dilated pulsating conus and gallop rhythm localized to the left second and third interspaces, with a rise in venous pressure, speak eloquently for a failure and dilatation of the right ventricle; the left remaining normal. In the reports on the " cor pulmonale " there are many instances of chronic enlargement and failure of the right heart in the presence of a normal left ventricle. Rogers (1908–1909) and Clarke *et al.* (1927) report cases in which the right ventricle was larger than the left, which was itself normal.

The following case is presented as one that falls into this group and shows that the right ventricle may fail for a long time without any appreciable failure of the left side.

CLINICAL COURSE

A woman of 73 was quite well until four years before her death, when she noticed increasing dyspnœa on exertion and swelling of the legs and abdomen. At her first admission to Addenbrooke's Hospital she was cyanosed and showed gross œdema of the legs and sacral area, and a large abdomen which was distended with ascitic fluid. The cervical veins were engorged and the liver

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was enlarged to three finger-breadths below the costal margin. Her heart, at this time, was not greatly enlarged, but there was some dullness to the right of the sternum. The pulmonary second sound was loud and slapping and there was a·long, harsh systolic murmur in the mitral area. The rhythm was regular.

She was re-admitted on nine occasions, on each of which the abdomen was tapped, sometimes several times. In between she was well enough to do a little light housework, such as sewing, peeling potatoes, or cooking. Although short of breath on slight exertion, the relative absence of dyspnœa in comparison with the gross congestive failure was very striking ; on one occasion she was able to walk into the ward with three gallons of fluid in her abdomen. Although she preferred the sitting posture, she was not in a true sense orthopnœic, and, except when the ascites was extreme, was able to lie flat without dyspnœa. During the whole time of observation, a period of some two years, she was deeply cyanosed and showed gross engorgement of the cervical veins. Although under continual treatment with mercurial diuretics, her œdema and ascites persisted, and the ascites was only temporarily relieved by tapping of the abdomen.

In the past she had been healthy and had never had rheumatic fever or chorea.

On examination on many occasions during the last two years of her life she showed the following signs.

She was emaciated and cyanosed, with many telangiectatic venules over the face, which was not unlike that of mitral stenosis. The cervical veins were engorged up to the level of the angles of the jaw and pulsated feebly ; they stood out as thick, knotted cords almost as thick as the little finger. Œdema and ascites were always present.

The pulse was regular and of small volume : the blood pressure, 110/85 mm. On her first admission the left border of the heart seemed normal and there was some dullness to the right of the sternum. Later the apex moved out a little, but the dullness to the right of the sternum disappeared. The heart was never greatly enlarged to clinical examination. In the mitral area there was a loud, rough systolic murmur ; the pulmonary second sound was increased ; the aortic sounds were normal ; and there was a systolic murmur in the tricuspid area. There was no pulsus paradoxus, no systolic retraction, no Broadbent's sign, nor any of the other signs attributable to an adherent pericardium.

Throughout her illness the chest appeared to be clear except for occasional rales at the bases. There was no pleural effusion.

On all her admissions the abdomen was tightly distended with fluid. The liver was greatly enlarged and was not tender to pressure apart from her first admission early in the disease; it appeared to be hard and smooth. The spleen could not be felt. The nervous system showed no abnormality.

Radioscopy four months before her death showed some enlargement of all the chambers of the heart, most marked in the right ventricle and left auricle. Pulsation was rather feeble and pulmonary congestion was said to be slight.

The electrocardiogram showed no abnormality apart from right ventricular preponderance. The circulation time (arm to tongue with suprachol) was

35 seconds. The Kahn reaction was negative. The lævulose tolerance test showed moderate liver deficiency.

Throughout the four years of her illness there was neither deterioration nor improvement ; she died suddenly for no apparent reason just after admission to hospital for tapping.

In view of the constant engorgement of the neck veins and the anasarca, a clinical diagnosis of chronic right heart failure of unknown cause was made.

AUTOPSY

An autopsy showed acute failure supervening on chronic failure of a hypertrophied right heart, and emphysema of the lungs.

Heart.—This showed great hypertrophy of the right ventricle and right auricle. The left ventricle did not look hypertrophied. Before the fat was removed the total heart weight was 15 oz. (425 g.). Differential weighing after separation of the ventricles and removal of all fat (Herrmann and Wilson, method B, 1921–22) showed that the right ventricle weighed 107 g., the left 127 g. This gave a left to right ventricular ratio of 1·19. Lewis (1913–1914) gives the normal average L/R ratio as 1·8, the limits of variation lying between 1·47 and 2·06. Herrmann and Wilson consider anything below 1·50 or above 2·20 as abnormal.

The normal figures for the weights of left and right ventricles are shown in the table (after Lewis and Herrmann and Wilson). As both these authors weighed the septum separately in their series, the figures below have been obtained by adding one third of the septal weight to the weight of the right ventricle and two thirds to that of the left.

	Weight of Ventricles in Grammes	
	Right	Left
Average (Herrmann and Wilson) ..	51	91
Average (Lewis)	56	100
Range (Lewis)	36 to 80	74 to 141
Present case	107	127

It will be seen that while the left ventricle may, at the most, have been slightly hypertrophied, its weight fell within the range of normal figures.

The right ventricle was extremely hypertrophied and was responsible for most of the increase in heart weight. The relationship between the size of the two ventricles is well seen in the coronal section of the heart shown in the figure on the next page.

Microscopy of the myocardium showed that the fibres in the right ventricle were greatly thickened, while those in the left were normal. In spite of the patient's age, atheroma was inconspicuous in the coronary arteries and aorta. On the other hand, there was severe atheroma in the pulmonary artery and its branches. Microscopy of the pulmonary arterioles showed no abnormality and no obstruction. The valves and pericardium were normal.
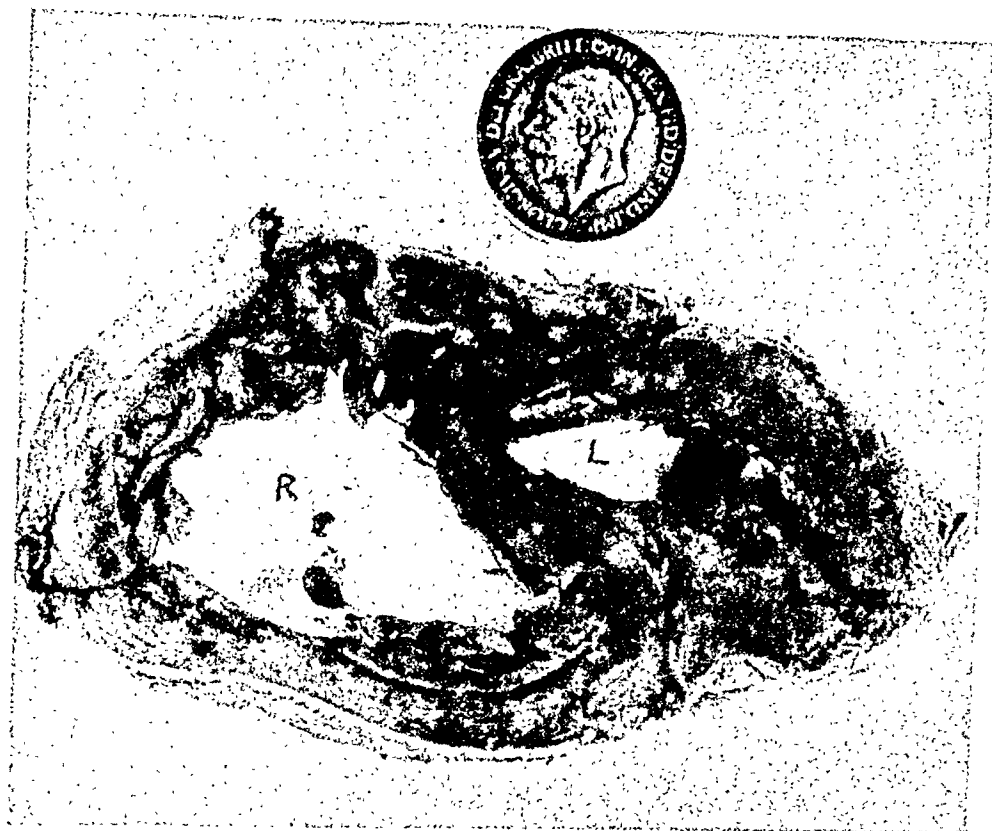
FIG. 1.—Coronal section of the heart.   Natural size.   R : right ventride.   L : left ventricle.
    Diameter of coin is one inch.

Lungs.—These were small, generally congested, and very œdematous ;
but this was probably terminal.   There were emphysematous bullæ along both
anterior borders.   Microscopically, the lungs showed a very fine, even emphy-
sema, with œdema, congestion, and phagocytosis of blood pigment.

Abdominal Organs.—The liver showed fibrous thickening of the capsule,
mainly over the antero-superior surface and the anterior border, with plaques of
hyaline " sugar icing " which could be stripped from the underlying organ with
moderate ease.   Microscopically and macroscopically there was fibrous thicken-
ing both of the portal systems and of the tissues around the central veins.   The
latter areas showed congestion.   The hepatic fibrosis, well marked in all
regions, showed its greatest intensity just beneath the capsule.   The larger
hepatic veins were widely patent and of quite abnormal cross-section.   All
were surrounded by a rim of fibrous thickening.

The sugar icing was composed of hyaline fibrous tissue and lay outside the
elastic fibres of the real capsule.   It had evidently been laid down from outside.
It is interesting that the changes in this liver were similar to those found in
eight cases of constrictive pericarditis that came to autopsy (Day and Armstrong,
1940).

The peritoneal cavity contained several pints of clear yellowish-brown fluid.
There was fibrous thickening with sugar icing all over the parietal peritoneum,

most marked anteriorly and less pronounced over the under-surface of the diaphragm. The spleen was congested and œdematous, with plaques of sugar icing on its surface. There was general fibrous thickening of the intestines, stomach, pancreas, and mesenteric and retro-peritoneal fatty tissues.

There was gross induration and œdema of the subcutaneous tissues. The remaining organs were normal.

DISCUSSION

The view that this patient suffered from a failure of the heart restricted to the right ventricle is based on a variety of clinical and pathological observations. In the first place, she suffered from right ventricular failure for at least two years, during which time personal observation revealed gross engorgement of the neck veins. Her relative lack of dyspnœa and orthopnœa, often in the face of gross ascites and œdema, is strong evidence against any material degree of pulmonary congestion caused by left ventricular failure.

The pathological findings present even stronger evidence. The left ventricle was normal in weight and in the thickness of its walls. Practically all the increase in weight of the heart was due to the right ventricle, which weighed nearly as much as the left. The muscle fibres of the right ventricle were greatly hypertrophied ; those of the left ventricle were normal in thickness. The slight degree of atheroma in the thoracic aorta was in keeping with the clinical finding of a low systemic blood pressure ; the conspicuous amount of atheroma in the larger pulmonary arteries suggested that the pulmonary arterial pressure must have been greatly above the normal. The chronic œdematous and fibrous changes in the lower part of the body and the hepatic congestion and fibrosis of " cardiac " type are proof that, in addition to compensating hypertrophy, there had also been a long-continued failure of the right side of the heart.

As in the cases reported by East (1940), the ultimate cause of the right ventricular failure remains obscure. There were no valvular lesions and no obstruction or narrowing of the pulmonary arterioles. The atheroma in the larger branches of the pulmonary circuit was evidently the result and not the cause of the hypertension. This is in accordance with the views of Rosenthal (1930), who states that primary sclerosis of the pulmonary arteries affects the arterioles most and the larger branches least ; secondary atherosclerosis, as in mitral stenosis (and as in this case), affects principally the large branches and leaves the arterioles unimpaired. It is possible that the emphysema was the cause of the obstruction, but it is unlikely in view of the relative mildness of the dyspnœa during life. Moreover, according to Parkinson (1937), right heart failure, when caused by emphysema uncomplicated by cardiovascular disease, is present only in the terminal phase a short while before death. Persistent or recurrent heart failure in emphysema is nearly always the result of coincident cardiac disease. As the heart of this patient had been failing for at least two years, it is unlikely that emphysema was the cause.

It is impossible to state whether pulmonary hypertension was the cause or the result of the right ventricular -hypertrophy. Perhaps the most likely

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hypothesis is that a local rise of pressure occurred in the pulmonary arteries as a result of spasm or some other unknown factor that left no mark upon the final pathology of the lungs, and that such isolated pulmonary hypertension occasioned hypertrophy and later failure of the right ventricle.

A survey of the papers on pulmonary arteriosclerosis, cor pulmonale, and the condition known as " Ayerza's syndrome " leads one to the conclusion that in a proportion of these cases no pathological explanation has yet been found for the right ventricular failure. Many cases (Arrilaga, 1913 ; Ribierre and Geroux, 1921 ; Warthin, 1919 ; and Clarke *et al.*, 1927) failed to show any arteriolar obstruction that could impede the pulmonary blood flow. Atheroma and medial degeneration of the larger arteries will not obstruct the flow owing to the relatively large size of the cross-section of these vessels : it is only when the lumen is relatively small that projections from its wall will cause obstruction. These cases showed atheroma and dilatation of the pulmonary arteries with normal arterioles, and in Warthin's case (a syphilitic) the smallest pulmonary vessels and even the pulmonary veins were dilated. This observation would appear to exclude a primary obstruction in the vessels themselves. These cases are mentioned to emphasize that there are some on record that show right ventricular hypertrophy without any adequate pathological explanation ; the clinical picture is, of course, quite different, for this patient was in no sense a " black cardiac." In the other cases of cor pulmonale a true endarteritis of the smaller vessels often accompanied by thrombosis (Rosenthal *et al.*, 1930) constitutes a real obstruction to the pulmonary circuit and would be expected to produce hypertension and hypertrophy of the right chambers of the heart. In a proportion of cases of cor pulmonale, however, it would seem that the pulmonary atheroma, as in the present case, was the result rather than the cause of the condition ; the exact ætiology of the cardiac hypertrophy remaining unknown.

Whatever the cause, it appears that in the case here reported the right heart failed alone, or at least greatly in excess of the left. Many other examples of preponderating right heart failure, but with a different symptomatology, are to be found in the papers mentioned.

The interest in this case lies, in particular, in the chronicity of the disease and the long-continued failure of the heart with a rise of the venous pressure. It would seem that the absence of left ventricular failure and pulmonary congestion was the reason for the extreme chronicity, and that this was the deciding factor in prolonging life. In most cases the left ventricle precedes the right in failure, and when the right heart fails it is a more transitory condition, relieved by treatment unless the patient dies. A series of attacks of right heart failure is common, but in the intervals the right heart remains efficient and the venous pressure is not above normal. It is suggested that in the presence of a failing left ventricle, right ventricular failure is not compatible with life for more than a limited period of time. It is only when the burden of pulmonary congestion is absent, that is when the right ventricle fails alone or at least greatly in excess of the left, that congestive cardiac failure can continue almost indefinitely. This hypothesis is in keeping with the observation that many patients with rheumatic tricuspid

disease live for a quite disproportionate time if the severity of the valvular lesions and the degree of failure are taken into account. The extra valvular lesion protects the lungs from flooding and, in rationing the left ventricle with blood, wards off the failure of this chamber. The same syndrome of long-continued right heart failure with persistent ascites is seen occasionally when an enormous enlargement of the right heart has taken place ; I have seen several such cases, but no autopsy was obtainable and the exact anatomical diagnosis of the cardiac lesions remained in doubt. The same result is seen in constrictive pericarditis—perhaps the most chronic of all forms of congestive failure—although here the heart itself does not fail, but is prevented from doing its work by outside factors. It is, none the less, a failure of right-sided type without pulmonary congestion. In conformity with the above hypothesis there is an unremitting heart failure of long duration. The similarity between constrictive pericarditis and the case recorded here hardly needs emphasis.

CONCLUSION

It is suggested, therefore, that the duration of the failure and its unremitting nature in this case were due to the right ventricle failing alone. The unusual pathological findings, the cardiac " cirrhosis " of the liver, and the chronic indurative changes in the peritoneum, were probably an expression of the extreme chronicity of the disease, and are strictly comparable with the findings in constrictive pericarditis.

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COARCTATION OF THE AORTA AT OR ABOVE THE ORIGIN OF THE LEFT SUBCLAVIAN ARTERY

BY

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Coarctation of the aorta, according to Evans (1933), was first described by Morgagni in 1760. Blackford (1928) cites Barié to the effect that the first case was recorded by Paris in 1791. Abbott (1928) wrote a comprehensive discussion of 200 reported cases with autopsies, and estimated the statistical incidence of the various anatomical abnormalities. Blackford (1928) estimated the incidence of coarctation of the aorta as 1 in every 1550 autopsies, with the frequency in males twice as great as in females.

The so-called adult and infantile types of coarctation were discussed by Parker and Dry (1938). In the former the constriction is localized abruptly in the region of the aortic isthmus ; the lumen may be completely closed, the collateral circulation is extensive, and a patent ductus is rare. The latter, on the other hand, is characterized by a diffuse constriction between the origin of the left subclavian artery and the attachment of a patent ductus arteriosus.

Of the several theories advanced to account for the malformation, Blackford's (1928) seems the most reasonable. He explains it as due to the absence, atrophy, or imperfect development of the fourth left branchial arch. The various diagnostic features (Eisenberg, 1938 ; Dock, 1932 ; Ernstene and Robins, 1931 ; Ferris, 1935 ; East, 1932 ; Amberg, 1932 ; Woltman and Shelden, 1927 ; Deneke, 1925 ; and Hamilton and Abbott, 1928) are all illustrated in our case, except that murmurs were absent over the intercostal vessels.

It is apparently a rare form of the so-called adult type in which the localized constriction of the aorta lies at or just proximal to the origin of the left subclavian artery. Only 15 instances of this type seem to have been reported. Abbott (1928) discussed the post-mortem findings in 7 such cases and Parker and Dry (1938) reported another with a necropsy. King (1937) collected 10 additional clinical examples ; the reports of only 6 of these were available to us and only 3, in our opinion, fall into this classification.

These cases differ from the usual type in that the left shoulder and arm are for the most part excluded from the distribution of high-pressure blood flow. Erosion of the ribs by enlarged intercostal arteries, which is often absent in the rare variety of coarctation, is confined to the right hemithorax.

DESCRIPTION OF THE CASE

A Puerto Rican labourer, 32 years of age, was referred to the Charity Hospital of Louisiana at New Orleans for a determination of employability. When first seen (November 2, 1939) he stated that four years before, when he had a broken wrist, he had been told that he had high blood pressure and had been advised to do light work only. For the past 18 months palpitation and dizziness had become progressively worse, and finally permitted only the easiest kind of work without discomfort. Dyspnœa appeared only on marked exertion. Precordial pain had never been felt. There was no history of rheumatic or syphilitic infection.

Examination showed a well-developed man of sthenic habitus, 157 cm. tall, and weighing 62·2 kg. The retinal arteries were tortuous and slightly compressed the veins at the arteriovenous crossings. The eye grounds as well as the lips and mucous membrane of the mouth showed a purplish cyanosis. Pronounced pulsation of both carotid arteries was present and also a synchronous bobbing of the head ; the tension was apparently equal and was increased above normal. The thyroid showed a moderate general enlargement without any nodules or bruit. Pulsation of the subclavian artery was palpable in the right supraclavicular fossa and was both visible and palpable below the clavicle. No corresponding pulsation was present in the left supraclavicular and infraclavicular fossæ. There was no visible or palpable pulsation in the suprasternal notch and no venous distention was present.

The apex beat was in the fifth space, 10 cm. from the midsternal line, and was well localized and forceful. The heart sounds at the apex were loud. ·The first sound was split, and a soft, blowing systolic murmur was present. The intensity of the second sound was moderately and equally increased in the aortic and pulmonary areas. A moderately loud, harsh systolic murmur in the aortic area was transmitted upward to the sternoclavicular joint and was not accompanied by a thrill. The rhythm was regular and the rate 88 per minute. The blood pressure was 154/78 in the right arm, 98/78 in the left arm, 84/78 in the right leg, and 90/80 in the left leg. A distant soft systolic murmur in the right scapular region was thought to be transmitted from the aortic area. No pulsations, murmurs, or thrills were detected over the intercostal vessels. The volume of the right radial pulse was considerably greater than that of the left. Compression of the left carotid artery failed to alter the character of the left radial pulse. There were no visible or palpable pulsations of the abdominal aorta. The pulsations of the femoral arteries were soft, equal, and synchronous. There was a distinct lag of these pulsations behind those of the right radial artery. They were synchronous, however, with those of the left radial artery. The pulsations of the posterior tibial and dorsalis pedis arteries were easily felt.

The muscular development of the right shoulder and arm was abnormally heavy. The circumference of the right upper arm was 3 cm. larger than that of the left, and the impression of asymmetrical muscular development was thus confirmed. The other physical findings were normal.

The red blood cell count was 5,500,000 per c.mm. and the hæmoglobin was 98 per cent. (Sahli). The urine and the renal output of phenolsulphonophtha-

lein were normal. The blood reactions for syphilis were negative. Radioscopy of the chest in the postero-anterior, left and right oblique, and lateral diameters showed marked cardiac enlargement, chiefly the left ventricle and the left auricle. There was also moderate enlargement of the pulmonary conus. A small aortic knob could be seen. The inferior borders of the dorsal segments of the ribs of the right hemithorax were eroded (Fig. 1). Barium in the
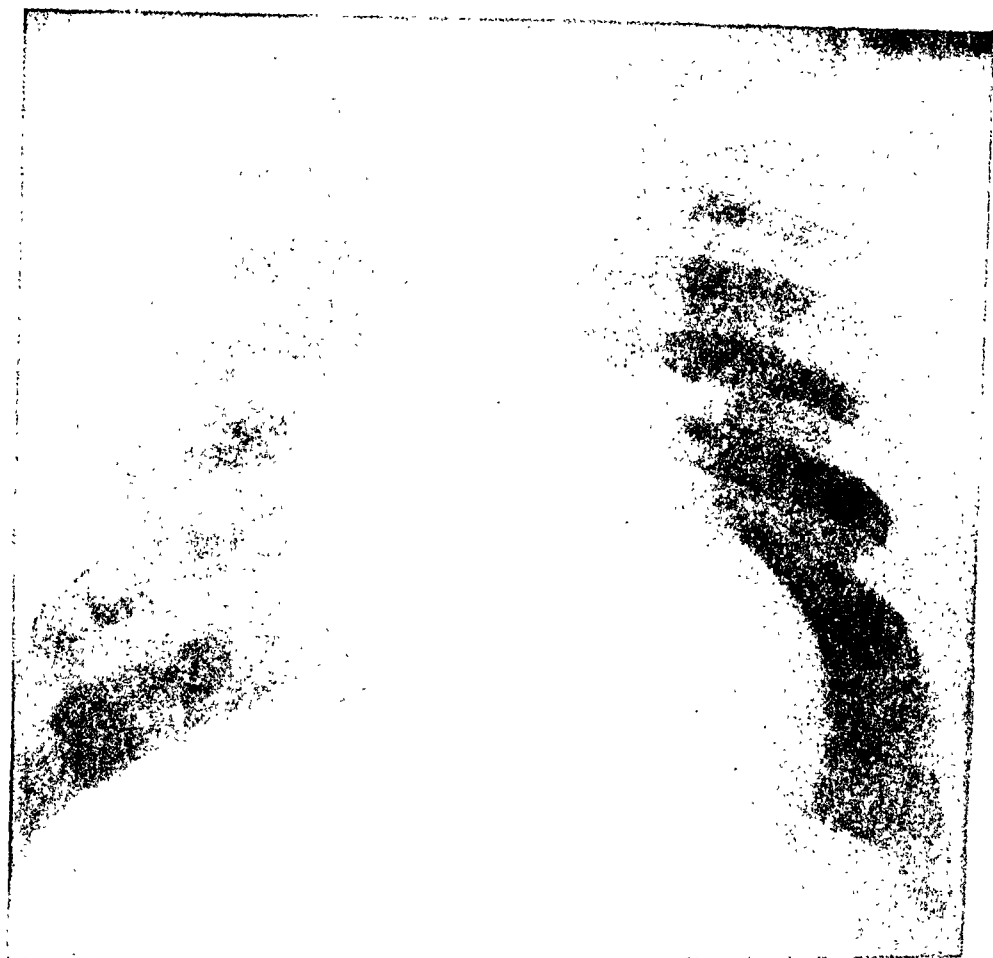
Fig. 1.—Radiogram, showing erosion of the ribs of the right hemithorax.

œsophagus confirmed these findings. Several attempts to visualize the aortic arch by taking radiographs of the chest following the injection of a 70 per cent. solution of diodrast into a large vein of the arm (Robb and Steinberg, 1939) were not very successful because of the abnormally small calibre of the deformed aortic segment (Fig. 2). Fig. 3, taken with a double string galvanometer of the Einthoven type, which recorded any two leads simultaneously, showed that the P–R interval was 0·16 sec. and the QRS duration 0·12 sec. The form of the curve indicated a complete left bundle branch block. From curves taken by pairing lead I, first with semidirect leads first over the right and then over the left ventricle, it was possible to determine (after the method of Wilson *et al.*,
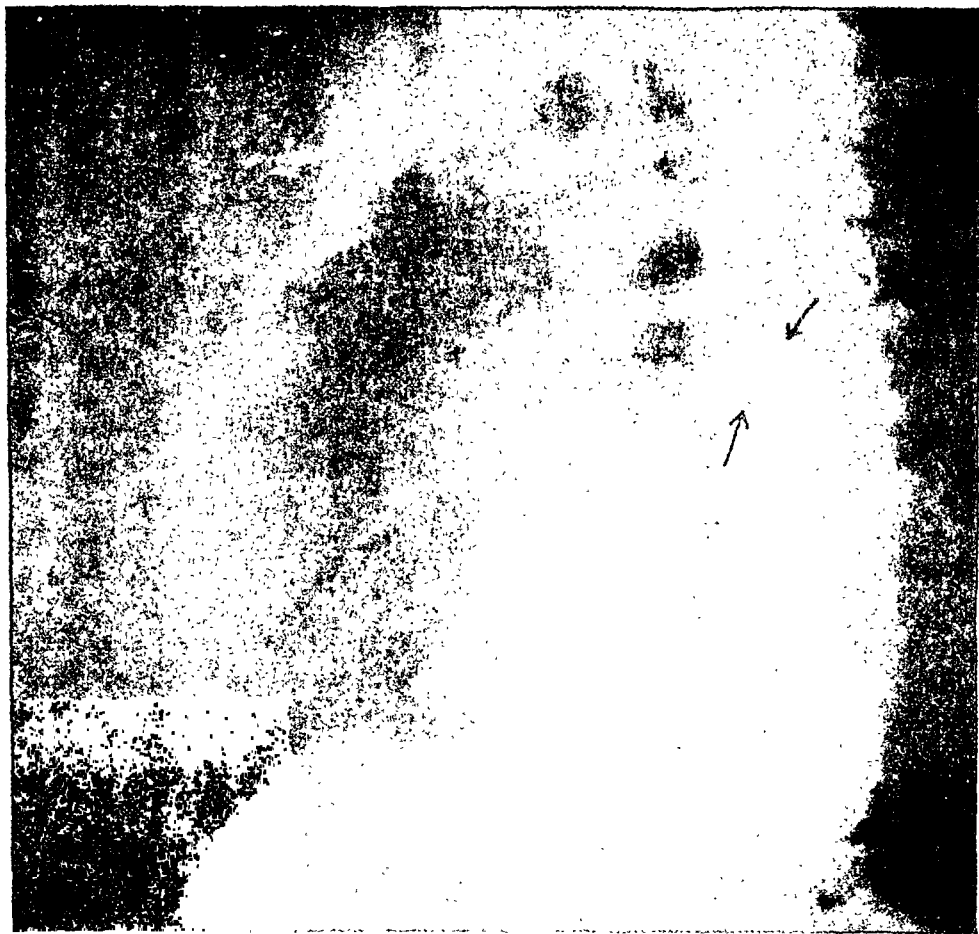
FIG. 2.—Second anterior oblique view showing the descending aorta beyond the stenotic region. Diodrast was used.
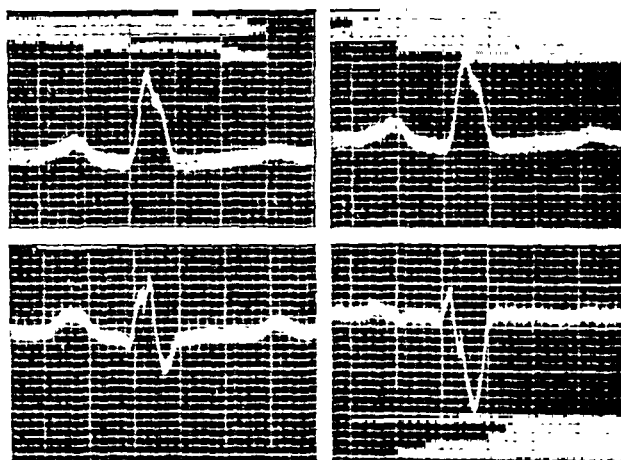
A   B

FIG. 3.—(A) Leads I and II recorded simultaneously. (B) Leads I and III recorded simultaneously. The standardizations, reading from above downwards and from right to left, are such that 1 mV. is equivalent to 1·0, 1·05, 1·1, and 1·25 cm., respectively. The small time division is 0·02 sec.

1932) that the accession wave arrived at the epicardial surface of the left ventricle 0·04 sec. later than at the epicardial surface of the right ventricle.

DISCUSSION

The clinical picture in this case is considered typical enough to establish the diagnosis of coarctation of the aorta. The difficulty found in attempts at radiographic visualization of the aortic arch was taken as evidence that this region of the vessel was hypoplastic. The basal systolic murmur can be explained by a trigonoidation (Chisholm, 1937) of the aortic semilunar valves or, in the same dynamic sense, on the basis of a bicuspid aortic valve. The presence of a left bundle branch block is not surprising, for this tends to appear in the ventricle subjected to the greatest strain (Bayley, 1934). This case is apparently the first of the kind to be reported in which erosion of the ribs was present. As might be expected, the erosion was confined to the right hemithorax.

Because of the striking difference in the volume of the radial pulse in the right as compared with that in the left arm, the rare variety should prove easier to differentiate from essential hypertension than the common variety of the adult type of coarctation. In both, the differentiation is important for therapeutics and prognosis. Simultaneous palpation of the radial and femoral pulsations is probably the most convenient method of routinely excluding aortic coarctation ; it would, however, seem unwise to rely on this procedure alone.

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PAROXYSMAL TACHYCARDIA CAUSED BY PENTAMETHYLENE-TETRAZOL

BY

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In 1930 Wolff, Parkinson, and White described the occurrence of bundle. branch block with a shortened P–R interval in persons with normal health, and subsequently other authors reported analogous cases. It has been generally assumed that no pathological significance, in the sense of a morbid affection of the cardiac muscle, should be ascribed to this electrocardiographic irregularity. A peculiarity noted by every observer, however, was that nearly all patients with this abnormality had at times either paroxysmal tachycardia or paroxysmal fibrillation or flutter.

In a schizophrenic patient in whom the bundle branch block with shortened P–R interval had been found, a paroxysm of tachycardia was observed four times, each time after an intravenous administration of pentamethylene-tetrazol. Three of the attacks were recorded.

A man, aged 43, was admitted to hospital in November 1937; he had been ill for half a year already with a diagnosis of schizophrenia. Physical examination revealed no peculiarities, neither did the examinations of the blood and spinal fluid. The blood pressure was 130/80. Roentgenologically the heart proved to be of normal size. In March, 1938, the treatment of schizophrenia by the production of convulsions with pentamethylene-tetrazol was started. Nine complete convulsive seizures were produced after intravenous administration of 5, 6, 7, or 8 c.c. of a 10 per cent. solution. The psychiatrist in charge did not observe any irregularity of the heart at the time; but after the first attack an increased pulse rate was noted (160 beats per minute). When, on May 3, I saw the patient, his pulse was still very high six hours after the tenth epileptic insult. The rate was not quite regular, and ranged between 160 and 170 beats per minute. The frequency of the heart was 206 beats per minute and entirely regular. There were no signs of decompensation. A more detailed examination was rendered impossible through the patient's negativism. The seizure was stopped through pressure on the eyeballs, the pulse rate falling to 82 beats per minute. The first cardiogram was taken the next day, and several others in the following months. As a rule, the P–R interval was shortened and QRS was widened with a negative T wave (see Fig. 2A):

Lead	P–R interval (seconds)	Width of QRS (seconds)	Total (seconds)
I	0·08	0·13	0·21
II	0·10	0·11	0·21
III	0·12	0·08	0·20

In each lead the P wave was positive and the T wave negative, while the ascending branch of the R wave always showed a notch. Occasionally alternating normal and abnormal complexes (Fig. 1A) could be observed, whereas now and then
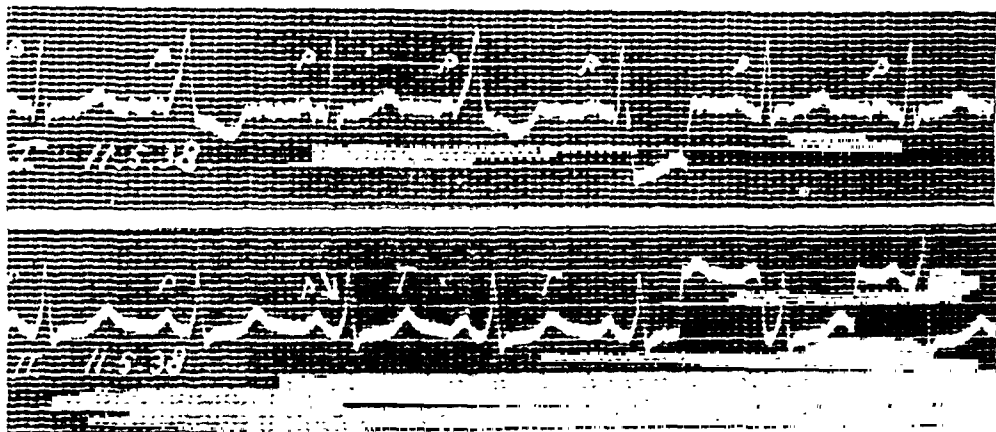
FIG. 1.—Normal rhythm. Lead I shows alternating normal and abnormal complexes. Lead II shows normal complexes with a P–R interval of 0·15 sec.

also normal complexes appeared persistently (Fig. 1B). In the normal complexes (lead II) the P–R interval amounted to 0·15 sec., the QRS width to 0·06, giving a total of 0·21 sec., which is the same as in the case of the abnormal complexes. In every one of them, however, the notch in the ascending branch of the R wave was noteworthy.

The abnormal electrocardiogram did not show any change after subcutaneous injections of 1 mg. of atropine, nor after bodily exertion.

In November, 1938, and in January and March, 1939, paroxysmal tachycardia was registered every time after intravenous administration of pentamethylene-tetrazol. As on the last occasion the insult of an attack was noted as well, and the electrocardiogram of that day is discussed below. The previous observations were similar. Fig. 2 was taken before the injection of 5 c.c. of a 10 per cent. solution of pentamethylene-tetrazol. The rhythm was roughly 90 beats per minute. After the injection at 11·16 no insult could be observed and only the cardiac rhythm had risen to about 106 beats per minute, the width of the QRS complex having fallen from 0·12 to 0·08–0·10 sec. After five minutes, 6 c.c. of a 10 per cent. solution were injected, which after twenty more seconds produced an insult with clonic and tonic cramps. Fig. 2B was taken as soon as possible. First two rapid beats were traced in succession. The P–R interval was 0·08–0·10 sec., the QRS width 0·08–0·10 sec., the T wave negative. After a pause a QRST complex of more normal type followed (QRS, 0·08 sec., T wave positive, but P–R interval (shortened to 0·10 sec.). After these there
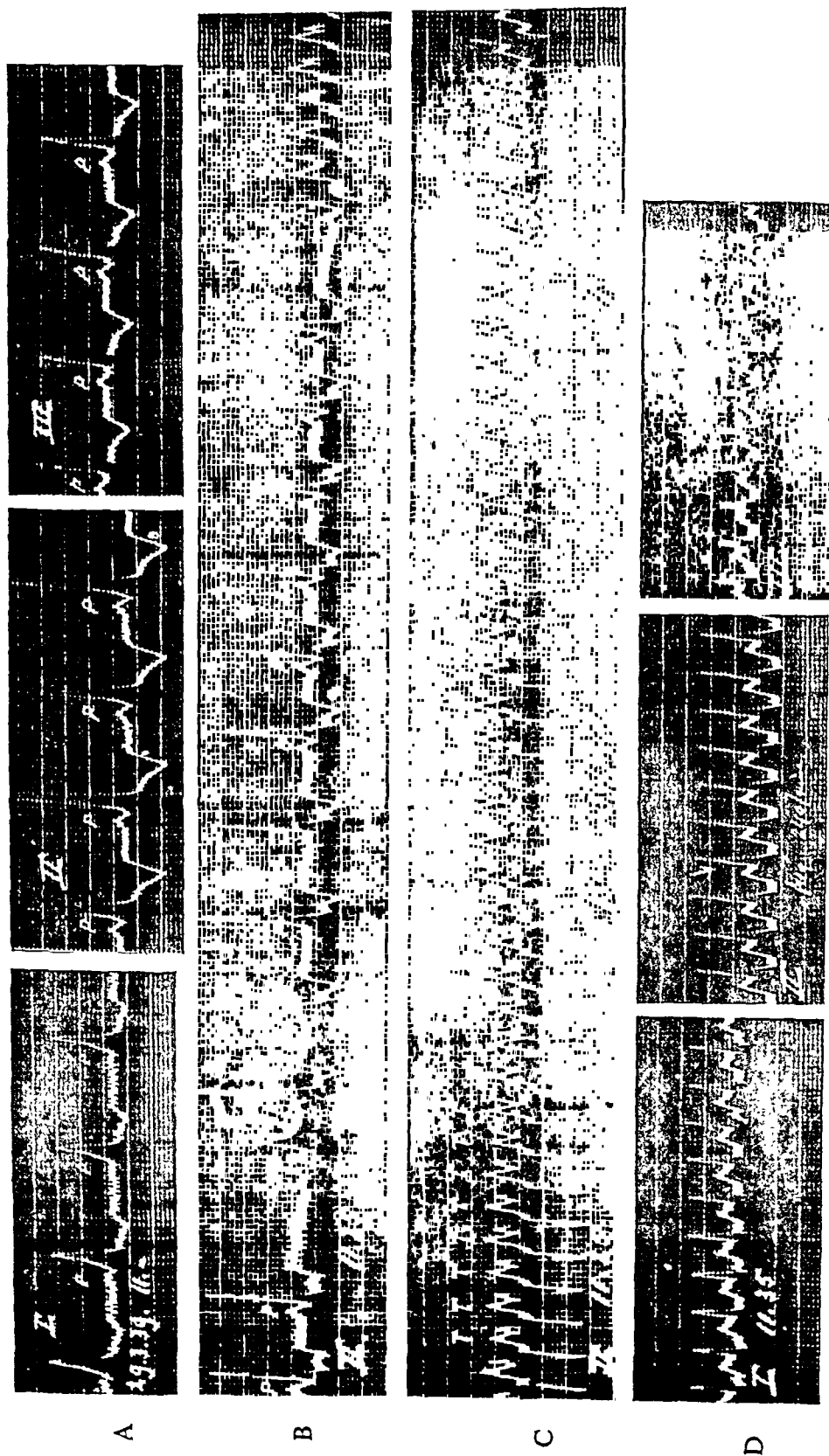
Fig. 2.—Before and during paroxysmal tachycardia on March 29, 1939. (A) shows the three leads before the injection of pentamethylene-tetrazol. (B), taken at 11.25 a.m., shows lead II four minutes after the second injection (see text) and, towards the end, the start of paroxysmal tachycardia, which is continued in (C). (D) shows the three leads during the paroxysm.

followed ten abnormal complexes, the tracing of which had not been entirely regular. The frequency of the last five amounted to 108 beats per minute. After another pause a complex was registered that resembled the one before these ten complexes and showed a P–R interval of 0·12 sec. Directly afterwards there followed an attack of ventricular complexes in a rapid succession (Fig. 2C). The frequency was 250 beats per minute, the QRS width about 0·08 sec., the T wave and the P wave doubtful. Suddenly an alteration in the aspect of the complex was observed, although the rhythm remained the same (see arrow, Fig. 2C): with a slight change (see Fig. 2D, lead II, and the beginning of Fig. 4A) this form was stationary.

The three leads (Fig. 2D) were registered during the paroxysm. The entire picture, especially the QRS complex, shows a great similarity to the pattern of the normal complexes which, for example, were to be seen after the end of the attack (Fig. 4D). Here too the notch in the R wave of II is striking (see arrow in lead II, Figs. 2D and 4D). The deviation is especially apparent in the ST interval, and is frequently observed with this disturbance (Scherf, 1937). P was nowhere to be recognized during the paroxysm (see Fig. 2D).

As regards the stopping of the attacks, the first of May 1938 was immediately abolished through pressure on the eyeballs. This was repeated whenever convulsion had set in, but it appeared that pressure of the eyeballs was only successful a few hours after the injection of pentamethylene-tetrazol. Pressure of the " carotid " was always violently resisted by the patient.

In Fig. 4A the first arrow indicates the moment at which the rhythm had become normal again. Initially, as is apparent from Figs. 4, A, B, and C, which link up with each other, the rhythm was irregular, viz. first slow and then quicker, with a few pauses of longer duration (Fig. 4C), in all probability the outcome of sinus arrhythmia; the P–R interval, which was first 0·08 sec., subsequently rose to 0·14–0·15 sec. In all complexes except the first two, R showed a notch. Remarkable, moreover, is the gradual return to normality of the pathological aspect of S–T, as is apparent in the four successive arrows in Fig. 4A. One ventricular extrasystole was registered.

The diagnosis made was paroxysmal auricular tachycardia. The sudden beginning and ending excluded sinus tachycardia, and flutter was highly improbable.

There is one more electrocardiagram we should like to discuss (see Fig. 3). It was taken just after stopping an attack in November 1938. In addition to an irregular rhythm, caused chiefly by a sino-auricular block, there appeared at the end of the curve a very brief fibrillation-flutter (see arrow).
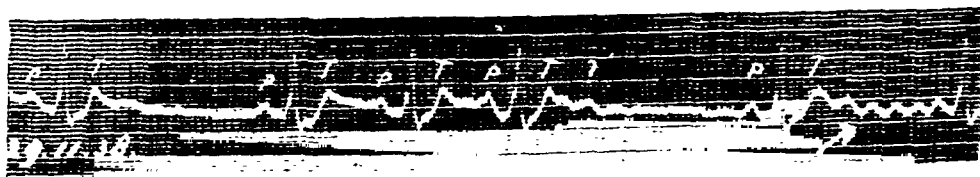
FIG. 3.—Normal rhythm shortly after stopping a paroxysm on November 29, 1938. At first the irregularity seems to be due to sino-auricular block, but later (at the arrow) there is a short period of impure flutter or coarse fibrillation.
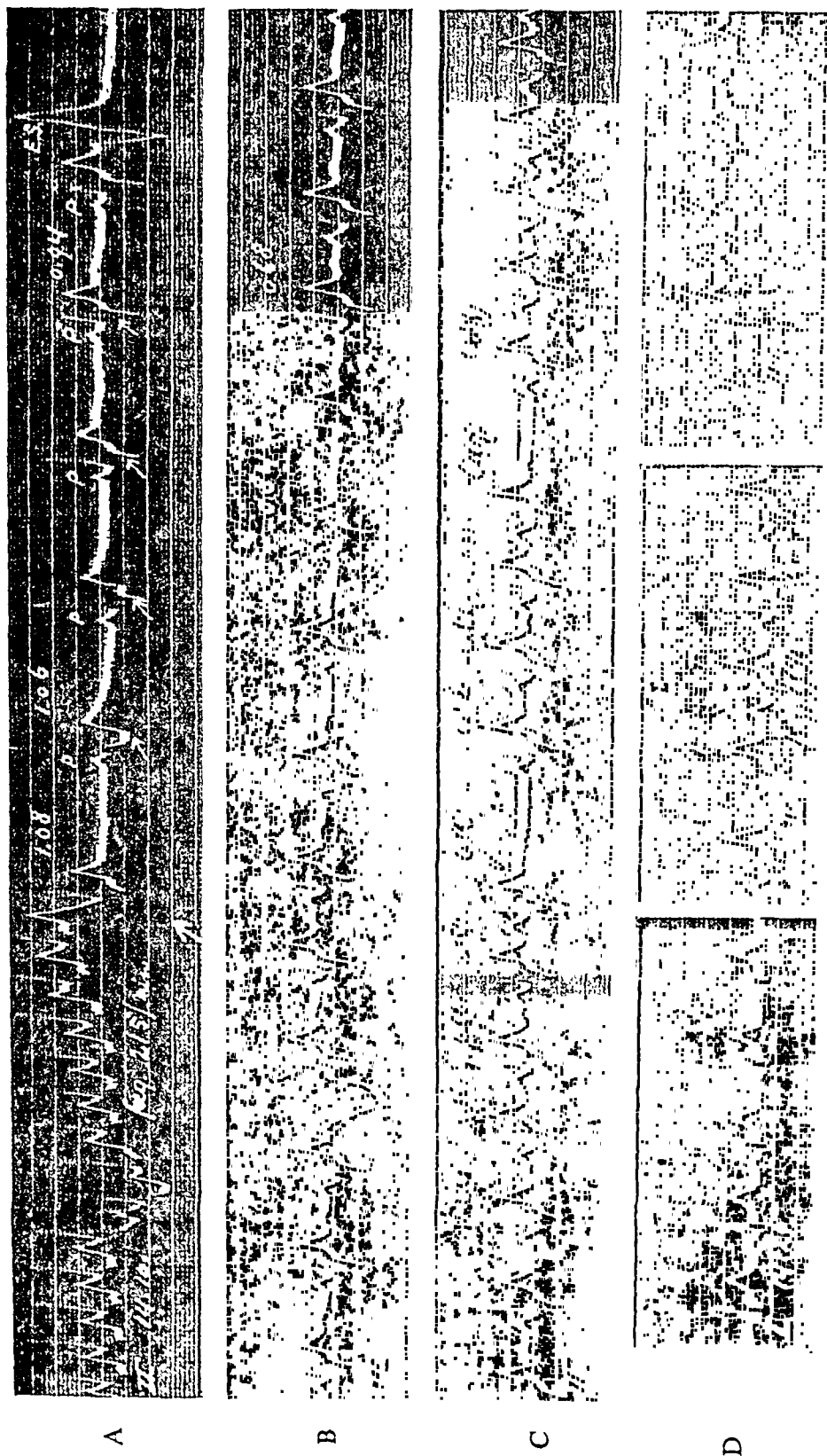
Fig. 4.—Immediately after the paroxysm on March 29, 1939. (A), (B) and (C), all lead II, were taken consecutively, starting at 2.10 p.m., and show an irregular rhythm, gradually becoming more normal (see text). (D) shows the three leads, taken ten minutes after the end of the attack, recorded in (A).

DISCUSSION

The cardiographic findings in this case are similar to those recorded previously. Here too, as indicated by Wolferth and Wood (1933), there could be observed the same interval from P to the end of the QRS complex both for the normal and abnormal complexes, and paroxysms of tachycardia with normal, non-widened ventricular complexes.

This instance is mentioned because pentamethylene-tetrazol proved capable of producing these attacks. Several drugs have been described as provoking paroxysmal tachycardia, such as digitalis (Schwab, 1931), quinidine (Lewis, 1921), adrenaline (Danielopolu, 1921), and atropine (Galli, 1918). The same was reported of pentamethylene-tetrazol ever since this drug was injected intravenously in doses of 0·3 to 0·8 g., as is usually the case when applying von Meduna's treatment. These attacks, which set in immediately after the insult, are of short duration (Géraudel, 1938) in most cases, the same as the irregularities observed, such as P, S–T, and T alterations and extrasystoles, block, etc. The longer duration of the attacks in the patient under consideration should be explained from the fact that he was predestined for such attacks, just as other patients with shortened P–R interval and bundle branch block.

Paroxysmal tachycardia may be caused—among other things—by the occurrence of an *accelerans-impulse* in connection with a sensitizing factor in the heart. Rothberger and Winterberg (1911) succeeded in obtaining this through injections of barium chloride into the cardiac muscle. In patients with shortened P–R interval and bundled branch block, however, this sensitizing factor is already present. As for the impulse from the accelerans nerve, the intravenous injection of pentamethylene-tetrazol nearly always gives rise to an accelerated rhythm of the heart even before the insult has been produced. Also in the case of our own patient, this acceleration could be noted (see Fig. 2).

Pentamethylene-tetrazol, therefore, if administered in the above quantity and manner was observed to produce the attack; in this patient, however, it appeared to be impossible to obtain the same result through an accelerated rhythm of the heart—100 and 110 beats per minute respectively—caused by bodily exertion or a subcutaneous injection of 1 mg. of adrenaline. Thus it ensues that, in all probability, the effect of pentamethylene-tetrazol should not be ascribed to the accelerans impulse exclusively.

As regards the pharmacological action of pentamethylene-tetrazol Hildebrandt (1937) stakes that as a result of the stimulation of the vasomotor centre the vagus centre is being stimulated as well. Camp (1928) demonstrated that pentamethylene-tetrazol in its effect on the autonomous centres of the brain is both a sympathetic and a parasympathetic stimulant. In view of the fact that Rothberger and Winterberg (1911) succeeded in developing paroxysmal tachycardia through electrical stimulation of vagus and sympathetic, it seems likely that the origin of such attacks after pentamethylene-tetrazol is to be found in a similar mechanism of stimulating vagus and sympathetic nerves. Lohr (1936) also accounted for the influence of adrenaline on the development of paroxysmal tachycardia in her experiments through a joint vagotonic and sympatheticotonic action.

We were unable to ascertain which is the mechanism concerned in the bringing about of spontaneous attacks in patients with shortened P–R interval and bundle branch block. Our patient developed an attack two days after the last insult without any medication. According to the family, he had never before suffered from any attack.

In the above we have limited ourselves to the discussion of the extracardiac influence of pentamethylene-tetrazol on the origin of these attacks. Nevertheless it is not improbable that the administration of much pentamethylene-tetrazol intravenously in reality does cause a lesion of the cardiac muscle. The irregularities observed by Géraudel (1938), Hoogerwerf and Jelerama (1938), and Forschbach (1939) point in this direction.

SUMMARY

In a patient suffering from schizophrenia, whose electrocardiogram showed a shortened P–R interval and a bundle branch block on four occasions, each time after an intravenous dose of 5.6 c.c. of 10 per cent. pentamethylene-tetrazol, an attack of paroxysmal tachycardia was observed, which after a few hours could be abolished by pressure on the eyeballs.

In connection with some further observations in this patient the probable explanation of the genesis of these attacks is discussed.

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THE INFLUENCE OF FEAR ON THE ELECTRO-CARDIOGRAM

BY

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While investigating the effect of an anæsthetic on the cardiac action, we chanced on the observation that fear of an impending operation produced remarkable changes in the electrocardiogram of many persons with normal hearts. We therefore proceeded to a systematic investigation in a larger number. Having reported some of these results (Mainzer and Krause, 1939), we are now adding further material, and trying to discuss the cardiographic and clinical significance of the findings.

The circulatory response of the organism, whether normal or pathological, to various psychic stimuli is a wide field of research that has been exhaustively investigated; and the influence of a psychic emotion, such as fear, on the cardiographic tracing forms only a small part of it. Nevertheless, there is such a striking parallelism between our electrocardiograms and the tracings obtained in coronary insufficiency or in myocardial damage that a discussion seems justified.

The electrocardiogram as induced by psychic emotion has been investigated by psychologists (Astruck, 1923 ; Landis and Slight, 1929 ; Weinberg, 1923). The results, which are mostly reported in the archives of psychology or psychiatry —including the paper of Blatz (1925), who is the only one to have studied the influence of fear on the electrocardiogram—are unfortunately not at our disposal. Bier (1930) found high P, R, and T waves after pleasant excitement in some of his experiments. The majority of workers used hypnosis to provoke emotional excitement.

Boas and Goldschmidt (1930), recording the pulse rate previous to and during surgical operations with Boas cardiotachometer, found it increased in frequency just before operation and instantly slowed down on the induction of general anæsthesia.

METHOD OF INVESTIGATION

The following procedure was taken in our examinations. In patients of the surgical or gynæcological departments of our hospital we recorded electrocardiograms : (1) one day before operation, the patient knowing nothing of the

impending operation ; (2) on the operating table just before the induction of general anæsthesia ; (3) while under anæsthesia ; and (4) on the day after operation or later, using an amplifier-electrocardiograph. The patients were recumbent, lying flat on their backs, and no drugs were given previous to the taking of the cardiogram. None of them was suffering from valvular disease of any kind or from any clinical symptom of congestive failure. We did not, however, exclude those patients who suffered from coronary sclerosis or arteriosclerotic muscular lesions. We recorded the tracings in the three classical leads. The standard gauge of amplitude was 1mV.=1·0 mm. The præcordial leads are not suitable for this kind of examination, since even a small displacement of the electrode placed near the heart in a second record may cause considerable modification of the tracing.

RESULTS

We made observations upon 58 persons, but the records of 5 of them could not be used for technical reasons. The findings obtained in the remaining 53 are shown in Table I.

TABLE I

ELECTROCARDIOGRAPHIC CHANGES INDUCED BY FEAR OF OPERATION

	Before Operation					
	Normal Records		Pathological Records		Total	
	M.	F.	M.	F.	M.	F.
No electrocardiographic changes induced by fear of operation ..	10	15	1	3	11	18
Electrocardiographic changes similar to those often seen in coronary insufficiency	0	12	1	4	1	16
Electrocardiographic changes as above, with P and T becoming larger and pointed also	1	3*	0	3	1	6*

* In one of these cases the change was in the P and T waves only.

The majority were women (40 females to 13 males). Twelve of the patients showed an abnormal tracing one day previous to the operation (rest-electrocardiogram) ; they were all suffering from coronary sclerosis, with the exception of one who was undernourished qualitatively as well as quantitatively (avitaminosis) owing to obstruction of the œsophagus through cancer. In 29 of the 53, four of whom had pathological tracings in the rest-electrocardiogram, the records taken immediately before operation were more or less unchanged. The remaining 24 showed pathologically changed tracings owing to fear of the impending operation.

The changes recorded can be classified into three groups :

(a) Those with changes that are most frequently encountered in coronary insufficiency—the S–T interval depressed below the iso-electric level (as compared

with the rest-electrocardiogram) ; the final wave T flattened or completely disappearing or becoming inverted ; S–T and T being deformed into a concave or convex curve ; more rarely, low voltage of the ventricular complex with notching; or a large Q in lead I or III. All these changes are found in more than one single lead.

(b) Those with changes that are usually met with in persons with neuro-circulatory asthenia or in connection with hyperthryoidism—the P and T waves becoming sharply pointed (as compared with the rest-electrocardiogram) and also showing increased voltage.

(c) Those with the changes described under (a) and (b) combined.

The changes of type (a)—as in coronary insufficiency—were encountered most often, i.e. in 15 patients, 4 of whom had already shown a pathological type of tracing at rest. Isolated changes of type (b)—as in persons with neuro-circulatory asthenia—were only found once. Combination of both types were more frequently present; i.e. in 6 persons, in 3 of whom the curve had already been abnormal previous to this.

As has been observed by Boas and Goldschmidt (1930), in the majority of cases a considerable acceleration of the pulse rate usually takes place previous to operation (see Table II), which, if it is very marked, may result in the fusion of the T with the P wave of the following contraction.

TABLE II

INCREASE OF PULSE RATE INDUCED BY FEAR OF OPERATION

Increase of Pulse Rate (per minute)	Nature of Record before Operation			
	Normal	Pathological	Normal	Pathological
	Without Changes of the Electrocardiogram		With Changes of the Electrocardiogram	
0–10	17	2	5	3
11–20..	2	1	2	1
21–30..	4	1	3	1
31–40..	2	0	3	1
Over 40	0	0	3	2
Total	25	4	16	8

These changes in the tracings, attributed to fear, make their appearance in the younger as well as in the higher age groups, though this might not be expected in view of the fact that in the higher age groups a greater incidence of coronary sclerosis and a tendency towards vasoconstrictor vagal action (Gilbert, 1923) prevail. Table III demonstrates that the younger age groups take their full share in this pathological response.

TABLE III

AGE OF THE 24 PATIENTS WITH CARDIOGRAPHIC CHANGES INDUCED BY FEAR

Age (years)	Before Operation	
	With Normal Records	With Pathological Records
Up to 30	12	1
31–40	2	0
41–50	0	3
Over 50	2	4

ILLUSTRATIVE CASES AND ELECTROCARDIOGRAMS

Some typical examples of the various types of " fear tracings " follow.

Fig. 1 shows a series of tracings of type (a), the rest-electrocardiogram of this case being normal. They are from a woman, aged 27, who was having an operation for appendicectomy.

The records taken on the day before operation (A) showed as the only remarkable feature an M-shape of the ventricular complex and a diphasic T in
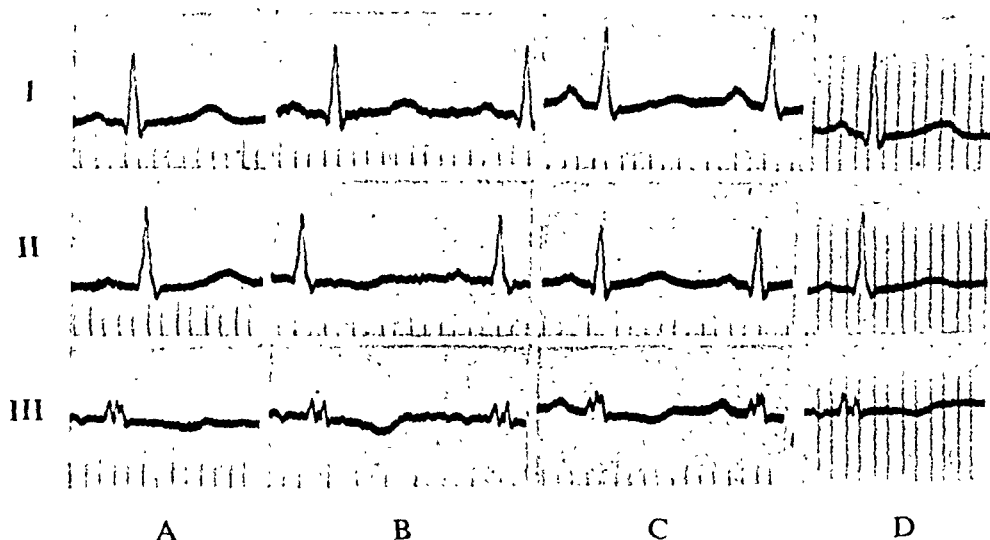
FIG. 1.—Electrocardiograms showing inversion of T_3 and partial inversion of T_2 as a result of anxiety.

(A) at rest ; (B) just before anæsthesia ; (C) during anæsthesia ; and (D) on the day after.

lead III. On the operating table (B) the S–T interval was below the iso-electric level, with a low voltage T in lead II and a negative T in lead III. As soon as general anæsthesia was induced (C) all these changes decreased in intensity. On the day after operation (D) the tracing more or less assumed the shape that had been found on the day before operation.

Fig. 2 shows how the pathological character of a record in coronary insufficiency may become accentuated. It is from a man, aged 70, who was having an operation for removal of the left stellate ganglion for gangrene of the fingers of the left hand. The rest-electrocardiogram of the day before operation (A) showed a slightly negative T_1 and an absent T_2, with S–T_2 and S–T_3 below the
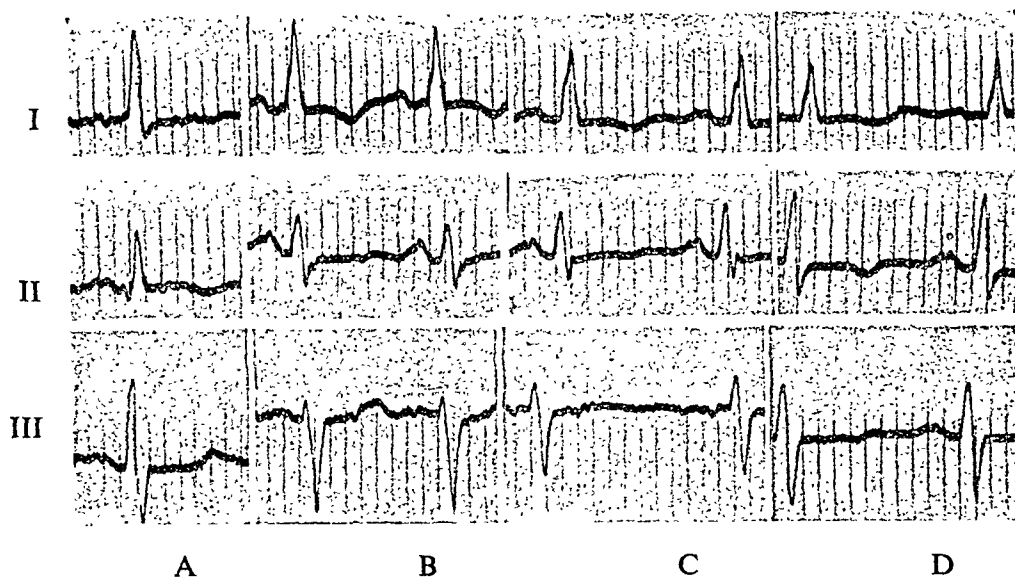
FIG. 2.—Electrocardiograms showing inversion of T_1 and partial inversion of T_2 as a
result of anxiety.

(A) at rest ; (B) just before anæsthesia ; (C) during anæsthesia ; and (D) on the day after.

iso-electric level. Immediately before operation (B) the tracing changed ; the
ventricular complex became pathological with left axis deviation that was not
previously observed, R_2 was much lower, S (of which there was only a trace
before) became distinct, and T_1 became negative and T_3 positive. Although
in this case too the pathological features induced by fear disappeared to a
certain extent during the anæsthesia, the tracing even on the following day
was not yet quite identical with the first record.

The only record of our material that may be considered a true represent-
ative of type (b) is shown in Fig. 3. It is from a woman, aged 25, who was
having an Alexander Adams operation for retroversion of the uterus.
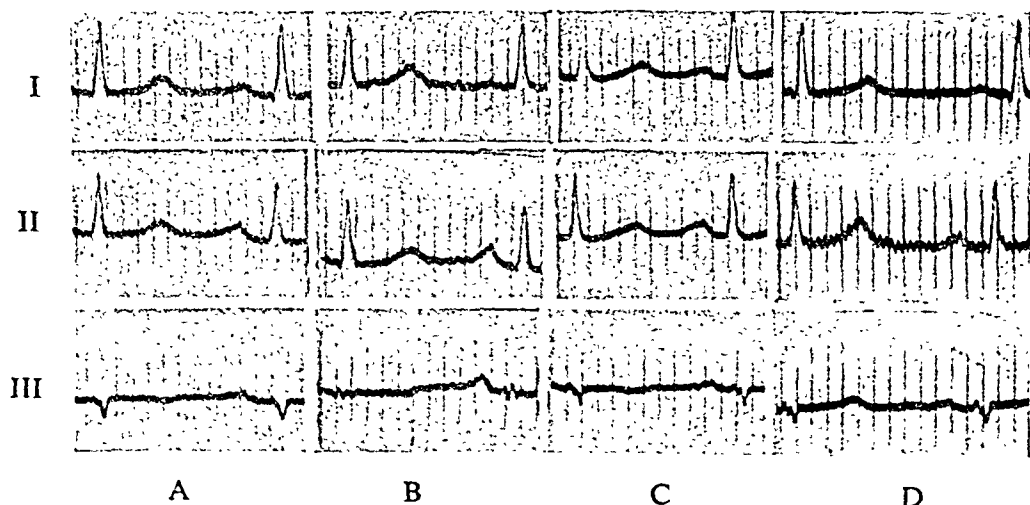
FIG. 3.—Electrocardiograms showing increase of P and T waves as the result of anxiety.
(A) at rest ; (B) just before anæsthesia ; (C) during anæsthesia ; and (D) on the day after.

The rest-electrocardiogram (A) showed no pathological features. The ventricular complex showed low voltage in lead III with T_3 negative. Immediately before operation (B) P_2 and even more P_3 increased in voltage and became more sharply pointed. At the same time the ventricular complex was lower, T_3 disappeared, and T_1 and, more markedly, T_2 became higher and more sharply pointed. In this case, too, the changes disappeared to a certain extent during anæsthesia (C). On the day after operation (D) the curve more or less assumed its original shape, save that there was a positive T wave in lead III.

Fig. 4 is characteristic of the combined type (*a*) and (*b*), so that the tracing becomes highly abnormal. It is from a man, aged 42, who was having a gastrectomy for a duodenal ulcer with obstruction of the pylorus.
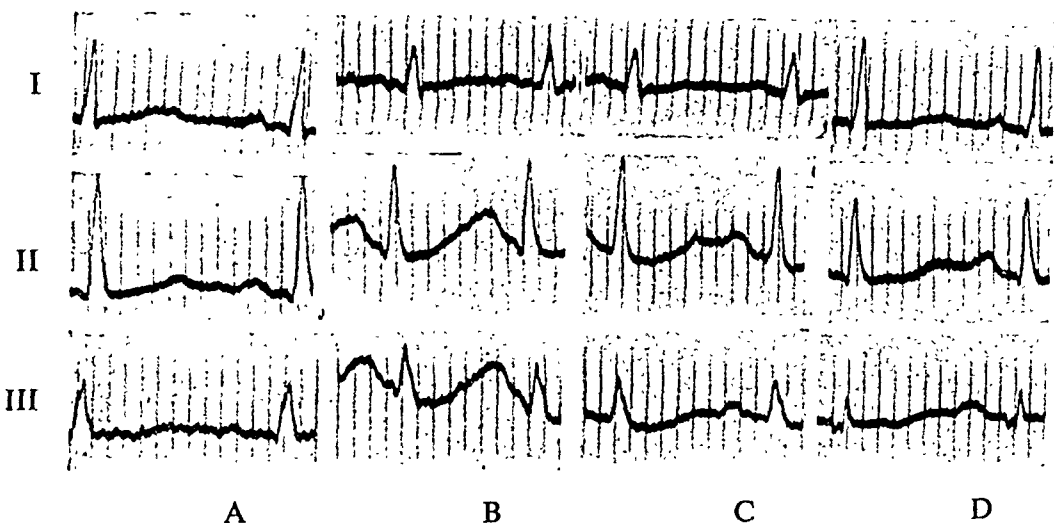
FIG. 4.—Electrocardiograms showing the earlier results combined as a result of anxiety. (A) at rest ; (B) just before anæsthesia ; (D) during anæsthesia ; and (D) on the day after.

The rest-electrocardiogram (A) of this patient may be called normal, T_1 being, however, broad and flat, and T_3 slightly inverted. The shape of this curve may have been influenced by a nutritional disorder (B-complex-avitaminosis). Immediately before the introduction of anæsthesia (B) very marked deformation existed ; in lead I, S–T and T were converted into a broad, slightly convex curve, and in leads II and III, the large T and the subsequent P formed one single large wave. During anæsthesia (C), however, the two deflections became separated to a certain degree. On the day after operation (D) the shape of the record had reverted even further, but not completely to the initial tracing; P_2 and P_3 remained high and T_3 had become negative.

In all these four cases there was an increased pulse rate before operation.

The question as to how long this " fear-reaction " of the electrocardiogram may persist has been repeatedly touched upon. In most of the remainder (17 of the 20 that showed the " fear-reaction "), a complete return of the curves to normal could be observed on the day following the operation.

The details are shown in Table IV. In 5 of these 25 patients, immediately after the induction of anæsthesia the tracing returned to its original shape. It is just as important, however, that in 3 further cases no return to the original curve took place, even after twenty-four hours.

TABLE IV

DURATION OF THE ELECTROCARDIOGRAPHIC CHANGES INDUCED BY FEAR

	Nature of Records before Operation		
	Normal	Pathological	Total
The deformation disappearing more or less during anæsthesia	1	4	5
The deformation disappearing on the day after operation..	13	4	17
The deformation not disappearing completely ..	0	3	3

THE SIGNIFICANCE OF THESE FINDINGS

When taking the records on the operating table just before the induction of general anæsthesia nothing in the proceeding or in the position of the patient differed from that used when taking the other tracings, except for the different psychic condition of the patients ; hence fear of the impending operation can be assumed to be the cause of the cardiographic changes. Moreover, no drugs were given. In five of these cases the elimination of consciousness alone (through anæsthesia) was enough to make the record return to its original shape—a further proof of the emotional origin of the cardiographic changes.

This circulatory response is obviously brought about by way of the autonomic nervous system ; the idea that it may be transmitted in a humoral way only is not compatible with the immediate disappearance of the reaction observed in five of our cases, as soon as the particular psychic strain subsided.

The cardiographic changes of type (*a*) are the same as those found in men (as well as in animals) with coronary insufficiency, and these are also, in part, of a transient nature. Gross anatomical changes concerning the position and the size of the heart or affecting the cardiac walls (pericarditis, myocarditis, etc.) can be excluded from the discussion in view of the transitory nature of the cardiographic alterations. It may, therefore, be assumed that the electro-cardiographic fear-reaction of type (*a*) corresponds to a reduced coronary circulation.

The problem of the vasomotor control of the coronary arteries is one of those intricate questions that can only be slightly touched upon here. If we assume (in accordance with Anrep, 1936 ; Wiggers, 1936 ; and Rein, 1931) that in the intact organism the coronary circulation is operated by the vagal tone, we may conclude that a vagal stimulus is responsible for the emotional restriction of the coronary flow. It is very tempting to conclude, on the other hand, that the increased pulse rate—as found in the reaction of type (*b*)—is produced by a sympathetic stimulus ; and that the mixed type of reaction (*c*)

may be brought about by the interaction of both factors. This interpretation remains hypothetical, since the coronary innervation has not yet been fully elucidated. Moreover, the interference of humoral factors cannot be disposed of, especially with reference to reactions of longer duration.

Their Importance for Clinical Cardiography

In clinical cardiography a certain number of records in persons with healthy hearts present a configuration of S–T and T approaching the borderline of the normal or even apparently pathological. Disturbances of internal secretion (ovarian insufficiency, deficiency diseases such as B-avitaminosis, or metabolic disorders) cannot be made responsible for these alterations of the tracing in every instance.

Many of these cases may in fact present fear-reactions, and clinically the fear may either become apparent (fear neurosis) or may remain hidden. Mainzer and Krause (1939) had the opportunity of recording three cardiograms of this kind. It would be a serious error to diagnose an organic heart disease on the grounds of such an abnormal tracing.

Sudden Death from Heart Failure Before and During Operation

Death on the operating table just before the induction of general anæsthesia (Dunbar, 1938) and deaths from cardiac failure during anæsthesia have often been reported. A transitory overdosage of the anæsthetic has been held responsible for the latter occurrence. However, a number of authors, (Hering, 1916), ascribe this event to the state of excitement provoked by the anæsthetic (chloroform) holding a vasomotor reaction (at least that taking place in the peripheral circulation) responsible for these fatal accidents (Alkan, 1930). Our observations, however, make it highly probable that these only represent the extreme cases of the otherwise ordinary fear-reaction, increased by the excitement while under the anæsthetic, and that coronary constriction must be considered the main factor.

Myocardial Damage of Neurogenic (Psychogenic) Origin

A number of clinicians have put forward the view that continuous or repeatedly recurring excitement is likely to advance organic lesions of the cardiac muscle or may even be active in producing them (Klemperer, 1929). This clinical theory of the neurogenic (psychogenic) production of muscular cardiac lesion has been supported to a certain degree by experimental work.

Manning, Hall, and Banting (1937) demonstrated that a prolonged vagal stimulation is able to produce congestion of the capillaries, extravasation of blood, and the development of hyaline foci of degeneration in the myocardium of the dog; and that the occurrence of these phenomena can be prevented by atropine. Even more marked were changes of this kind which Hall, Ettinger, and Banting (1936) were able to induce in the myocardium by administering the vagal substance, acetylcholin, to animals. In older animals this procedure will call forth multiple thromboses within the coronary area and myocardial

infarction as well as foci of hyaline or fatty degeneration with fibrous scar formation. In younger animals the arterial changes are absent and the myocardial damage is less pronounced ; in this case too atropine prevents their occurrence.

When transferring the results of these experiments to human pathology the objection might be raised that in the animal experiment the vagal stimulus and the acetylcholin dosage reached an unphysiological degree. In human pathology, however, similar observations have been made in connection with angina pectoris.

Ordinary angina pectoris is of transient nature, clinically and often electrocardiographically too. It subsides just as quickly as the psychic emotion before operation and the resultant circulatory response. Various investigators during the last decade have shown that, in spite of this transient character, the paroxysm of angina pectoris may give rise to the formation of circumscribed myocardial necrosis, which, in the course of time, may be converted into fibrous scar tissue (Gallavardin, 1932 ; Büchner, 1932 ; Holzmann, 1937). If, therefore, the heart has been subjected to a considerable number of attacks, the myocardium may be riddled with necrotic or, later, fibrous foci of microscopical size. As pointed out above, the vasomotor fear-reaction of the cardiographic type (*a*) shows a perfect analogy with that provoked by the angina pectoris paroxysm. If this is correct, the animal experiment as well as the clinical and pathological findings should lead us to envisage the probability that the emotional vagal reaction may also produce permanent anatomical lesion of the myocardium, the extent of which may depend on the degree and the frequency of the reaction.

Thus, our findings support in a certain degree the clinical hypothesis of a psychogenic origin of organic cardiac diseases.

Summary

On the operating table immediately before induction of general anæsthesia, an abnormal electrocardiographic record was found to develop in roughly two fifths of 53 cases, in comparison with the tracing of the previous day. These alterations were observed in persons with cardiac disorders, where they merely accentuated the pathological character of the cardiogram already existing, and also occurred frequently in patients with normal cardiograms. While in a number of patients the changes disappeared under the anæsthetic, or at least by the next day, they were in some cases still encountered twenty-four hours after operation.

The changes may be classified into three groups :

(*a*) S–T is depressed below the iso-electric level, and T is low, inverted, or absent altogether, S–T and T showing some deformation similar to that appearing in coronary insufficiency ;

(*b*) P and T are high and become sharply pointed, as is also found in neuro-circulatory asthenia :

(*c*) a combination of the changes quoted under (*a*) and (*b*).

Factors likely to modify the records, other than the excitement owing to fear of the impending operation, can be ruled out. In some patients the curve returns to its original shape even while they are still under the anæsthetic, thus supporting the hypothesis of a fear reaction.

In view of the analogies existing between " fear-electrocardiograms ". and other types of tracings, it is assumed that the curves of type (a) are brought about by a reduced coronary flow, mainly to be attributed to vagal stimulation ; that sympathetic stimulation is responsible for the development of the curves of type (b) ; and that type (c) is the result of the interaction of both factors. It is improbable that only humoral factors could be active in bringing about these phenomena, in view of their rapid disappearance.

Thus in clinical cardiography a number of abnormal records that can be explained in no other way probably present genuine fear-tracings, particularly where neurotic persons are concerned.

Death from cardiac failure on the operating table immediately before the induction of general anæsthesia as well as during anæsthesia should, therefore, at least in some cases, be considered as the extreme outcome of an otherwise usual fear-reaction.

The coronary spasms of an ordinary attack of angina pectoris may give rise to the formation of microscopically recognizable necrotic foci in the myocardium. Neurogenic (vagal) lesions of the coronary arteries and myocardium have also been encountered in animal experiment. Thus myocardial damage could be induced by the vasomotor fear-reaction, as becomes apparent in the curves of type (a), and could be attributed to coronary constriction of vagal origin.

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CARDIOVASCULAR DISTURBANCES CAUSED BY DEFICIENCY OF VITAMIN B₁

BY

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Deficiency of vitamin B_1 causes two distinct sets of signs and symptoms, affecting either the cardiovascular system or the nervous system. In their extreme forms these conditions constitute " wet " and " dry " beri-beri. Although both systems are commonly affected, it is usual for one to dominate the clinical picture. Beri-beri is still a frequent cause of illness and death in China, Japan, the Philippine Islands, the East Indies, and Brazil ; in the last few years attention has been drawn to its occurrence in the United States of America. In England gross deficiency of vitamin B_1 is rare, but mild and subclinical states are probably fairly common.

The studies of Wenckebach (1934) upon so-called " beri-beri heart " in Java and of Keefer (1930) in China have been admirably extended by Soma Weiss and his colleagues ; in Boston cardiovascular disturbances, due probably to deficiency of vitamin B_1, are not uncommon; they occurred in a ratio of about 1 in 160 admissions to the medical wards, and were more frequent than congenital heart disease or subacute bacterial endocarditis (Weiss and Wilkins, 1937). Few cases have been reported in this country. One of us described two cases of cardiovascular disturbances associated with low blood vitamin B_1 to the Association of Physicians in 1938 (Sinclair, 1938), and nine cases more recently (Sinclair, 1939, c). Six cases with heart failure or œdema and significantly low values for vitamin B_1 diphosphate ester in the blood have also been reported (Goodhart and Sinclair, 1940). Price (1938) recorded a case of wet beri-beri associated with chronic alcoholism and a deficient diet, and Garrett (1938) a case of " polyneuritis with œdema simulating beri-beri " which he did not believe to be due to a vitamin deficiency. Yudkin (1938) described a case of wet beri-beri in an Indian living in London on a diet mainly of rice ; no vitamin B_1 was found in his urine before treatment. Wood (1939) has discussed two cases ; Jones and Bramwell (1939) have recently described a case of " alcoholic beri-beri " responding to treatment with vitamin B_1 ; and Boyd Campbell and Allison (1940) have reported a case of beri-beri (polyneuritis and changes in the electrocardiogram) combined with pellagra in Belfast.

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The following three cases are reported because they were diagnosed as wet beri-beri on clinical grounds, and responded well to therapy with vitamin B_1 ; two of them gave very low values of this vitamin in the blood before treatment, but in the third this was not estimated.

CASE 1. BERI-BERI IN A CHRONIC ALCOHOLIC

A florist, aged 39, was admitted to hospital on September 9, 1936. His first symptoms, 15 months previously, were pains in the legs and numbness of the feet. Bilateral foot drop then developed, and for one year he could only walk with sticks. Six months before admission swelling of the legs and short-ness of breath added to his troubles, but he continued at work, serving in his shop until August. The shortness of breath was then evident even at rest, and cough disturbed his sleep.

For 17 years he had drunk about six pints of beer or stout daily. His appetite, though never large, had begun to fail in recent weeks.

On examination he was of a ruddy complexion with slight cyanosis of the lips. Tense œdema extended half way up the thighs and round the sacrum. Orthopnœa was urgent, and the cervical veins were engorged up to the angle of the jaw in the sitting position.

The brachial and radial arteries felt normal for his age, and no changes were visible in the retinal arteries. The blood pressure was 135/80 mm. The pulse was regular and the rate 120. The apex beat was felt three quarters of an inch external to the left nipple line. The heart sounds were tic-tac in quality, and no murmurs were heard.

The respirations were 23 per minute, and coarse rales were heard over both lung bases. The liver was tender and extended down to the umbilicus. Both grips, and flexion and extension of the elbows, were weak. There was bilateral foot-drop and tenderness of the calves. ·The knee and ankle jerks were absent. Sensation to cotton wool and pinprick was impaired over both forearms and legs, and also over the front of the chest and lumbar region. The urine con-tained no albumen or sugar.

X-ray (Fig. 1 A) showed considerable broadening of the heart shadow to the left and right, and the left contour suggested enlargement of the left ventricle. The hilar shadows were unduly stressed, as were also the vascular markings in the lung fields. Four examinations of the sputum were negative for tubercle bacilli. Wassermann and Kahn reactions were negative.

A fractional test meal showed complete achlorhydria, and the same test repeated after histamine injection showed absence of hydrochloric acid except in two samples, which were neutralized by 10 c.c. of N/10 NaOH.

Progress.—The patient was kept at rest in bed on a restricted salt and fluid intake ; his alcohol was stopped. and a diet adequate in vitamin B_1, containing two eggs per diem, was given. The dyspnœa and œdema decreased. The enlargement of the heart disappeared within a month, and still further reduction had taken place three months later (Fig. 1 B). The pulse rate, which was at first 120. declined to 80 in eight days.

A   B
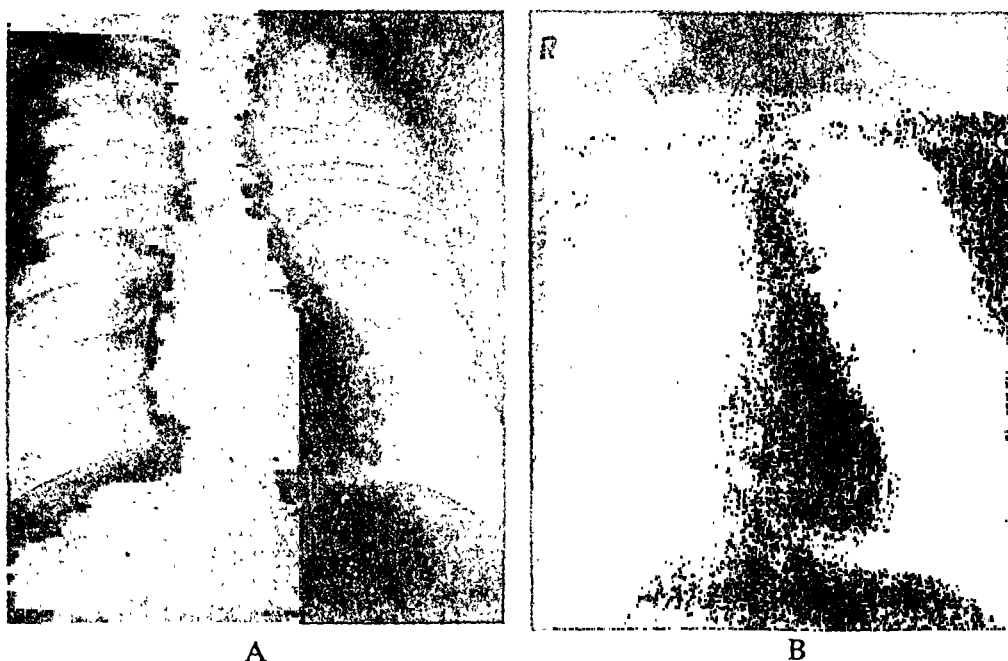
FIG. 1.—Case 1. Radiograms before and after treatment.

(A) September 11. The transverse diameter of the heart is much increased to the right and left ; considerable pulmonary congestion is present.

On September 22 the transverse diameter of the heart has considerably diminished (by 2·2 cm.) and the pulmonary congestion has disappeared.

(B) December 22. The transverse diameter of the heart is still further reduced, the total reduction of the transverse diameter being 3 cm.

This and the films in Fig. 2 have been taken with a standard technique, but were not teleradiograms.

The limbs, however, remained painful, tender, and weak; and as alcoholism had probably caused the peripheral neuritis, it was decided to try vitamin B_1 therapy. At that time Strauss (1935) and others in America had established the identity of alcoholic peripheral neuritis with beri-beri, and Russell (1936) in Scotland had successfully treated certain cases of peripheral neuritis with vitamin B_1. One of Russell's patients had clinical evidence of enlargement of the heart and " heart attacks." The possibility of the cardiovascular changes in this case being also due to beri-beri was then considered ; Weiss and Wilkins had published their findings in the same year (1936).

On October 10, 1936, daily injections of vitamin B_1 (500 units) were begun, and in addition marmite ʒ i, t.i.d., was given orally. In 11 days the injections were reduced to one on alternate days. By this time considerable subjective improvement had occurred : the appetite returned ; there was no dyspnœa or œdema, and the liver was only just palpable ; the pains in his limbs had disappeared and the muscles were less tender. Motor power took longer to recover, but on his discharge from hospital, in November, he no longer had foot drop and the power of his arms had recovered ; the knee and the left ankle jerks had returned, but were sluggish ; the right ankle jerk was still absent.

When seen in January both knee jerks and ankle jerks were brisk. He was walking well, and there was no tenderness of the calves.

CASE 2.   BERI-BERI AND SUB-SCURVY WITH MALNUTRITION AND
ACHLORHYDRIA

A metal dealer, aged 42, came to hospital on May 27, 1938.   Owing to bad trade he had been on a poor diet, mainly bread and margarine, though once or twice a week he would have corned beef and a little vegetable ; he took no eggs, salads, or fruit ; he was a teetotaller.   His ankles had begun to swell 18 months before, and a week before coming to hospital increasing shortness of breath was noted—even on talking.   For five days he had noticed weakness and numbness of both legs.   He also complained of swelling of the gums, looseness of the teeth, and intermittent attacks of epigastric pain, relieved by vomiting.

He was thin and dyspnœic, and pitting œdema extended up to the knees. The gums were spongy and bled easily.   The cervical veins were slightly engorged, but there was no orthopnœa.

The pulse was 110 and regular   The radial, brachial, and retinal arteries were normal for his age, and the blood pressure was 120/80.   The apex beat was in the mid-clavicular line and the heart sounds were normal.   No abnormal physical signs were detected over the lungs or in the abdomen.   Motor power in the legs was moderately impaired.   The knee jerks were present, but the ankle jerks were difficult to elicit.   The calves were somewhat wasted and tender ; objectively sensation was not impaired to cotton wool or pinprick over the lower limbs.

The heart was enlarged to the left and right, and there was evidence of pulmonary congestion in the hilar and basal regions (Fig. 2A).

No tubercle bacilli were found in the sputum.   The fractional test meal, with and without histamine, showed complete achlorhydria.   The blood count showed no anæmia and no abnormality.   The Wassermann reaction was negative.   The specific gravity of the urine was 1022 and there was no albumin or sugar.

Progress.—The patient was kept at rest in bed on an ordinary hospital diet containing fruit juices for five days, whilst investigations were being made, including the estimation of the vitamin B$_1$ in the blood.   As this was found to be very low (2·5 ug per 100 c.c. blood), he was then given 2 mg. of vitamin B$_1$ (Benerva–Roche) by intramuscular injection daily for 18 days, after which the injections were continued on alternate days for five weeks and then twice a week for another two months.   During this latter period 2 mg. of aneurin were given daily in the form of Benerva tablets.   Marmite ʒ i, t.i.d., was given for four weeks.

He improved steadily, the dyspnœa disappearing in one week and the œdema in a fortnight.   The pulse rate fell from 110 to 80, and the transverse diameter of the heart, as seen in the radiogram (Fig. 2B), showed a considerable decrease in 17 days.   The vascular congestion in the hilar and basal regions of the lungs had also disappeared.

Unfortunately an electrocardiogram was not taken until 18 days after beginning vitamin B$_1$ therapy.   It showed an inverted T in lead III, and this had become flat a month later.

On discharge from hospital in July he was feeling well and the gums no longer bled.   The weakness of his legs and the tenderness of his calves had

A   B

FIG. 2.—Case 2.   Radiograms before and after treatment.

(A) May 28.   The transverse diameter of the heart is increased, with pulmonary congestion.

(B) June 14.   Reduction of transverse diameter of heart.   The evidence of pulmonary congestion has disappeared.

disappeared ; the ankle jerks, however, remained sluggish.   Vitamin therapy was continued.

CASE 3.   BERI-BERI AND CIRRHOSIS OF THE LIVER, IN A CHRONIC ALCOHOLIC

A publican, aged 35, was first seen on March 31, 1939.   For six years he had been short of breath and had been forced to give up playing games.   For a year he had been tremulous and for two weeks he had complained of pains in his legs and swelling of the ankles.

His appetite had always been small and in recent weeks had deteriorated. Morning cough and vomiting had troubled him for 18 months, and for 6 months he had suffered from recurring epistaxis.   He took no breakfast.   He had been in the habit of drinking 10 pints of beer and 2 or 3 ounces of whiskey, and of smoking 20 cigarettes per day.   Apart from this there was nothing significant in his past history.

On examination, he was stout, and both ankles pitted on pressure.   His eyes were prominent, but he asserted that they had been so ever since he could remember.   There was no associated enlargement of the thyroid gland, but there was some tremor of the hands.   His basal metabolic rate was later found to be −16 per cent.   The exertion of getting undressed caused him to become short of breath, and the veins of the neck in the sitting position were distended up to the angle of the jaw.   The pulse rate was 115 and the rhythm was regular. His arteries appeared normal for his age.   The blood pressure was 130/100 mm. The apex beat could not be felt, but on percussion there was no evidence of

enlargement of the heart. A soft systolic murmur was heard over the base of the heart.

No adventitious sounds were heard over the lungs. The abdomen was prominent, and the rounded lower border of the liver could be felt five finger-breadths below the costal margin ; the surface felt rough and firm in con-sistency. The calves were tender, the left knee jerk was more sluggish than the right. The ankle jerks were absent. Sensation to cotton wool and pinprick was diminished on the medial side of both legs and ankles.

A teleradiogram showed a high position of the diaphragm. The heart was in the horizontal position, but did not appear to be enlarged. There was evidence of pulmonary vascular engorgement. The specific gravity of the urine was 1020 and there was no sugar and no albumin.

Pending further investigations, he was advised to continue with the same diet and intake of alcohol, and he was admitted to the West London Hospital on April 4. The vitamin B_1 content of the blood was found to be very low (1·5 μg. per 100 c.c.).

Estimation of ascorbic acid in urine : volume 75 c.c. ; 2·8 mg. per 100 c.c. ; total acid 2·1 mg.

A fractional test meal showed absence of free hydrochloric acid until the last two specimens, taken at 90 and 120 minutes, the highest reading being equivalent to 25 c.c. N/10 NaOH.

Progress.—His intake of alcohol was then stopped. Marmite ʒ i, t.i.d., was given by mouth, and also injections of 1000 units of vitamin B_1 (Benerva) were given on alternate days, and eleven days later daily.
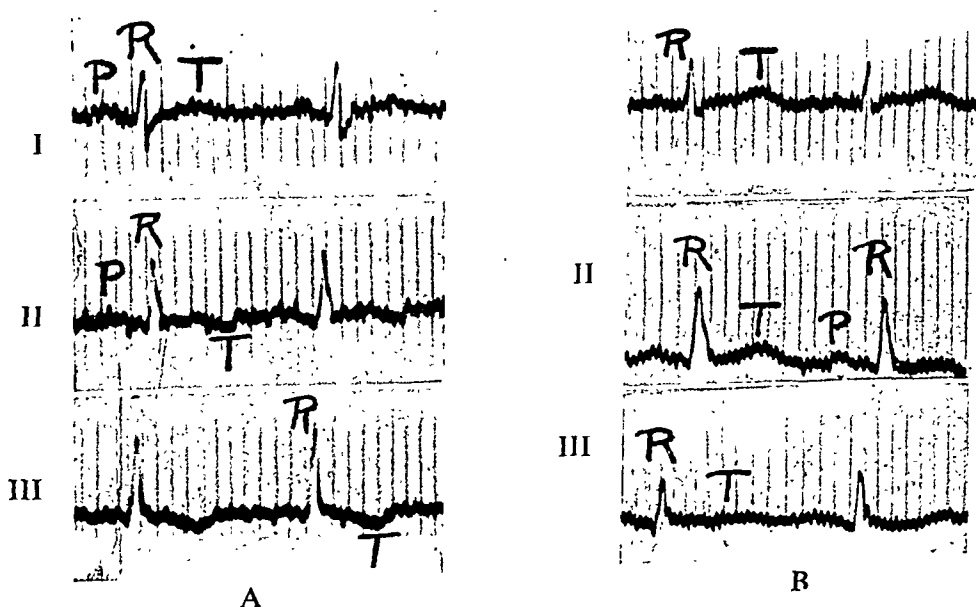
FIG. 3.—Case 3. Electrocardiograms. Time intervals 0.05 sec. Standard calibration.
(A) April 14. Sinus tachycardia, rate 100. T_2 and T_3 are negative.
(B) May 25. T_2 is now positive. T_3 is flat. T_1 is higher voltage. The tendency to right axis deviation has disappeared (see page 237).

The œdema and engorgement of the cervical veins disappeared at the end of two weeks. The pulse rate remained raised, averaging about 98. The liver decreased in size, and its lower border could only be felt three finger-breadths below the costal margin, two weeks after his admission; the size then remained unaltered, and the firmness of the organ gave the impression of cirrhosis. The pains in the legs and the hypoalgesia took about a month to disappear. On discharge from hospital in May the knee jerks were rather more brisk, but the ankle jerks remained absent. The vitamin B_1 content of the blood had risen to the normal figure of 8·5 μg. per 100 c.c.

A cardiogram taken on March 31 showed an inverted T in lead III and another on April 14 (Fig. 3A) showed a tendency to right axis deviation, with a negative T wave in leads II and III. Another taken on May 2 showed that the axis deviation had disappeared ; T in lead II was now flat, but T in lead III remained negative. On May 25, T in lead II had become positive, whilst T in lead III had become flat (Fig. 3B).

X-ray repeated on May 19 showed disappearance of the pulmonary vascular congestion ; the transverse diameter of the heart was almost unaltered, but the diaphragm was lower.

<center>DISCUSSION</center>

Certain features are common to these three cases. All complained of dyspnœa and of swelling of the legs ; all had mild neuritis in the legs with tender calf muscles ; all had tachycardia and achlorhydria (or marked hypochlorhydria). Two gave a history of chronic alcoholism and had enlarged livers ; two had enlarged hearts with venous congestion but without albuminuria, hypertension, arteriosclerosis, signs of syphilis, or a history of rheumatic fever, Vitamin B_1 was estimated in the blood of two and found to be very low in amount ; all three improved after therapy with vitamin B_1.

It is customary, following Aalsmeer and Wenckebach (1929), to describe three forms of cardiac change due to deficiency of vitamin B_1 : first, a mild form occurring in ambulatory patients and accompanied by dyspnœa, palpitation, tachycardia, and slight dilatation of the right side of the heart ; secondly, a moderately severe form accompanied by œdema, mild polyneuritis, and enlarged heart and liver and spleen ; thirdly, an acute pernicious form (*shōshin*) accompanied by sudden congestive failure, præcordial distress localized to the sternum, extreme dyspnœa, and a greatly dilated heart. While the term " beriberi heart " is ascribed to any of these three forms, deficiency of vitamin B_1 can cause either neuritis without any cardiovascular disturbance or œdema without any obvious disturbance of the heart. We are not here concerned with the ætiology of famine œdema, which is probably usually due to dietary deficiency of protein. Schittenhelm and Schlecht (1919), in an outbreak in a German labour corps, attributed the œdema to the low protein and high salt content of the diet, and failed to cure it with vitamin B. On the other hand, Jansen (1920) found that the protein intake was not abnormally low in another series of cases in Germany. Whereas famine œdema is typically accompanied by a decrease in the plasma albumin and bradycardia or no cardiac disturbance

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in wet beri-beri the plasma albumin is usually normal and cardiac disturbances (including tachycardia) are very frequent.   The three cases described here belong to the moderately severe type of cardiac disturbance, although in one there was no evidence of cardiac enlargement.

The diagnosis in these cases rests upon four features : the clinical characteristics, the dietetic evidence of deficiency of vitamin B_1, the response to therapy, and the estimation of the vitamin in the blood.

Clinical Characteristics

The commonest cardiac symptoms of deficiency of vitamin B_1 are dyspnœa on exertion, palpitation, and tachycardia.   Œdema, gallop or " tic-tac " rhythm of the heart, and " pistol shots " heard over the peripheral arteries are common.   The last sign, like the decreased circulation time, is due to the widespread peripheral arteriolar dilatation and is only found associated with congestive heart failure in deficiency of vitamin B_1, in Graves' disease, and in fevers. The presence of most of these features in our three cases and the absence of evidence of other forms of organic heart disease suggest the diagnosis.

Following Wenckebach and Aalsmeer, whose cases were observed in the Orient, there has been a tendency to speak of right-sided failure.   In the United States and in England there has been no uniformity of the clinical picture.   The failure may be peripheral, or if central is often right- and left-sided ; the pulmonary vascular congestion in Cases 1 and 2 (Figs. 1 and 2) demonstrates the left ventricular stress.

The heart may be normal in size or much enlarged.   Diuresis, reduction in the tachycardia, and often a hyperactive carotid sinus reflex are early signs of improvement.   The rapid reduction in the transverse diameter of the heart is well seen in Figs. 1–2, and is comparable to that which occurs in the myxœdema heart when it is responding to thyroid medication.   The peripheral neuritis responds less dramatically to vitamin B_1 therapy ; subjective improvement occurs early, but the signs usually take many weeks to disappear.

Electrocardiographic Changes.—Aalsmeer and Wenckebach (1928) and Wenckebach (1934) noted shortening of the P–R interval (0·12 sec. or less) in inhabitants of Java suffering from beri-beri.   Other observers, notably Keefer (1930) in China and Weiss and Wilkins (1937) in the United States, have analysed series of cardiograms in beri-beri subjects.   Feil (1936) reported on 38 cases of pellagra, but noted that the cardiographic changes were similar to those occurring in beri-beri ; possibly due to associated beri-beri.   The chief abnormalities were sinus tachycardia, flattening or negativity of the T waves, prolongaton of the Q–T interval (electrical systole), low voltage QRS waves, ventricular or auricular extrasystoles, and changes in the electrical axis either to the right or left. Mainzer and Krause (1940) also reported on 23 pellagrins, in about three fifths of whom the cardiograms were abnormal ; although the changes were similar to those in beri-beri, they emphasized the return to normal in some cases subsequent to nicotinic acid treatment : there was, however, no mention of the vitamin B_1 content of the hospital diet.

Electrocardiograms were not taken in Cases 1 and 2 until four and three weeks after admission to hospital, and by this time no striking changes were present. Case 3 showed sinus tachycardia, transient tendency to right axis deviation, and negative T waves in leads II and III.

Dustin *et al.* (1939) have called attention to the increasing abnormality of the cardiograms in some cases during the first week or two of treatment. Case 3 showed this interesting sequence of events ; in the first cardiogram, taken on March 31 (not reproduced here), there were no T wave changes or axis deviation, although subsequent curves showed them (Fig. 3).

Dietetic Evidence. The Cause of Deficiency of Vitamin B_1

This has been discussed at length elsewhere (Sinclair, 1939, *a*). The requirement of the vitamin varies directly with the metabolism of the body and the ingestion of carbohydrate (or alcohol) (Cowgill, 1934) ; for this reason inanition alone does not produce deficiency. Deficiency is therefore commonest in young male adults ; particularly those who ingest large amounts or carbohydrate or of alcohol. These three patients were males aged between 35 and 42 years ; two of them gave a history of chronic alcoholism, and the diet of the third consisted mainly of bread and margarine ; all three lived on diets that were deficient in vitamin B_1. If severe neuritis limits the patient's activity, cardiac disturbances are less likely : in two of the cases the neuritis was slight, and the third was at work although he could only walk with the aid of sticks. Deficiency of vitamin B_1 tends to occur in those with gastric achlorhydria because the vitamin is easily destroyed in an alkaline medium (there is no evidence that the deficiency causes achlorhydria) : all these three had achlorhydria or marked hypochlorhydria. Further, there is evidence that liver damage impairs the utilization of vitamin B_1 because the liver is the main site of phosphorylation of the vitamin : two of these patients had enlarged livers. These factors provided adequate causes for a deficiency of vitamin B_1.

Response to Therapy

All three cases responded convincingly to therapy with vitamin B_1. It is obvious that the effect of therapy was not controlled : the patients were rested in bed and given an adequate diet without alcohol and containing marmite. Case 1, however, made much quicker progress to full recovery as soon as vitamin B_1 was administered parenterally (and marmite orally) ; Case 2 was kept on a hospital diet for five days before the vitamin was administered parenterally. The importance of parenteral administration of the vitamin, particularly in cases with achlorhydria, was shown by the case published by Laurent and Sinclair (1938), in which large amounts of the vitamin by mouth failed to cure the neuritis or raise the blood vitamin to normal. There can be little doubt that in the three cases described above full removal of the cardiac and neuritic symptoms was due to therapy with vitamin B_1. Since vitamin deficiencies are almost always multiple, controlled therapy is seldom justified, and any associated deficiency state such as pellagra, scurvy, or anæmia should receive appropriate treatment.

Vitamin B_1 in the Blood

In two of the cases the amount of vitamin B_1 in the blood was estimated by the modification of Meiklejohn's method recently described (Sinclair, 1939, b) ; a value of 4·5 μg. per 100 c.c. or less is significantly low. Very low values (1·5 and 2·5 μg. per 100 c.c.) were found in the two cases before treatment, and a normal value (8·5 μg.) was found in one case after treatment. There is a direct correlation between the amount of vitamin B_1 and the red cell count in the blood (Goodhart and Sinclair, 1940), but in the cases described in this paper the cell count was within normal limits. There is no doubt, therefore, that these two patients were grossly deficient in vitamin B_1. This fact, combined with the evidence presented above, strongly suggests that the cardiovascular disturbances in these three patients were caused by deficiency of vitamin B_1.

SUMMARY

1. Three cases of cardiovascular disturbances caused by deficiency of vitamin B_1, all living in Greater London, have been reported.

2. In two the diagnosis was confirmed by finding a very low amount of vitamin B_1 in the blood ; in the third no vitamin estimation was done.

3. Two of the patients were chronic alcoholics, and in one of these cirrhosis of the liver was present. The third lived on a very poor diet with a relatively high carbohydrate content. All three suffered from peripheral neuritis.

4. Achlorhydria or hypochlorhydria was present in all the cases.

5. The diagnosis, the reaction to treatment, the influence of diet and alcohol, and other associated factors have been discussed.

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A CASE OF BERI-BERI HEART

BY

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Reports of cases of heart failure due to vitamin B_1 deficiency in this country are still scanty enough to justify the publication of a single case. This one was made more interesting by being due, apparently, to a pure dietary deficiency, unconditioned by alcoholism or gastro-intestinal disease.

History of Patient

An unemployed bachelor, aged 55, was admitted on December 5, 1939, under the care of Dr. F. J. Nattrass, complaining of widespread œdema. He stated that about three weeks previously his legs and arms had begun to swell. He could not go to bed, as he lived alone, and he went about with the swelling rapidly increasing. About a week after the onset of the œdema he noticed that he was breathless on exertion for the first time. His previous illnesses consisted of a war wound in the left leg, an attack of hæmaturia in 1915, and a winter cough for the past twenty years. He had been out of work since July 1939 and his total weekly income was said to be 17 shillings, out of which he paid 8 shillings rent. He did his own catering and cooking. Details of his diet will be given below.

On admission he had severe œdema involving the legs, external genitals, and arms; there was considerable ascites. There was no respiratory distress at rest. The pulse was regular, 94 per minute, and the blood pressure was 140/85 mm.

The chest was emphysematous and the size of the heart could not be ascertained. There were no abnormal heart sounds. There was dullness towards both lung bases, but this may have been due to œdema of the back. There were no adventitious breath sounds. The liver was not palpably enlarged or tender. The retinal vessels appeared normal. All the deep reflexes were active and there was no sensory loss. The skin was not pigmented. The urine was acid with a specific gravity of 1018 and contained no albumin or sugar.

The possibility of vitamin B_1 deficiency was considered at the outset, in view of the clinical picture of widespread œdema without any satisfactory evidence of cardiac or renal disease, and the fact that the patient was living under conditions that would be likely to produce avitaminosis.

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Treatment and course

On admission he received 2 c.c. of salyrgan intramuscularly, but no diuresis ensued. On the fourth day a test dose of 2 mg. of vitamin B_1 in the form of " betaxan " was given intramuscularly. The effect on the urinary output will be seen in Fig. 1. There was no result for twenty-four hours, after which the output rose quickly to reach a maximum of 160 oz. on the fifth day after the injection. The œdema rapidly subsided and at the end of ten days he was free
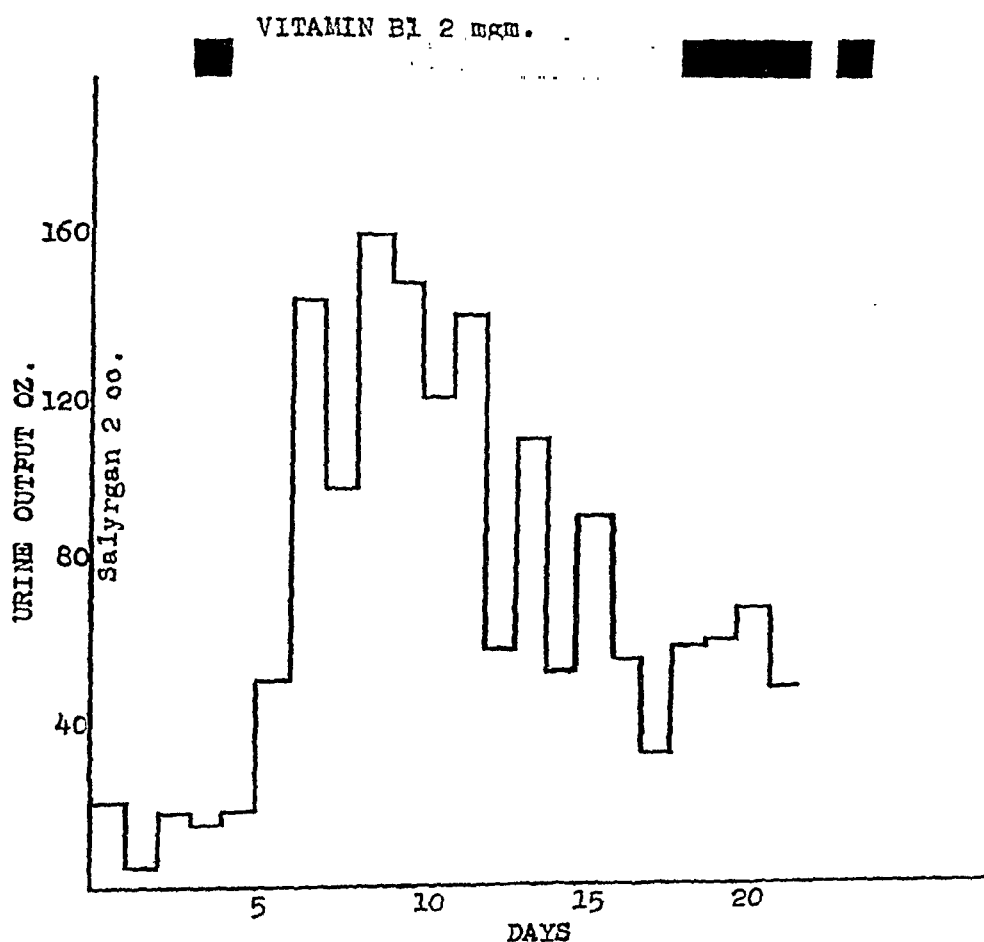
FIG. 1.—The urinary output following twenty-four hours after the initial test dose of 2 mg. of vitamin B_1.

from it and felt perfectly well. Vitamin B_1 was continued in 2 mg. doses and he received in all 32 mg. He was given ordinary hospital diet all the time and after the test period was over marmite was added.

He left hospital on February 6, 1940, free from all symptoms, and has remained well up to the present time.

Special Investigations

Radiological.—A teleradiogram (Fig. 2 A) taken on December 8 before any treatment had been given showed a considerable increase in the width of the heart

Fig. 2.—Teleradiograms before and after treatment with vitamin B₁.

(A) December 8, 1939, before treatment: note the large heart and some pulmonary hilar congestion.
(B) December 21, 1939, after 11 days' treatment: note the smaller heart and the disappearance of pulmonary congestion.
(C) January 23, 1940, after further treatment: note the continued diminution in the size of the heart and its return to normal.

shadow to right and left, with pulmonary congestion, more marked on the right side. Eleven days after treatment with vitamin B_1 had been started and at a time when improvement had set in the width of the heart shadow had decreased and pulmonary congestion was absent (Fig. 2 B). A third teleradiogram (Fig. 2 C), taken on January 23, 1940, showed a further decrease of the heart shadow to within normal limits.

Electrocardiographic.—A record taken on December 6, immediately after admission, showed a P–R interval of 0·12 sec. and rather low voltage QRS complexes ; T was flat in lead III and flattened and diphasic in leads I and II. On December 21, eleven days after treatment with vitamin B_1 had been started, the P–R interval was 0·16 sec., the voltage of the QRS complexes had increased,

A   B   C
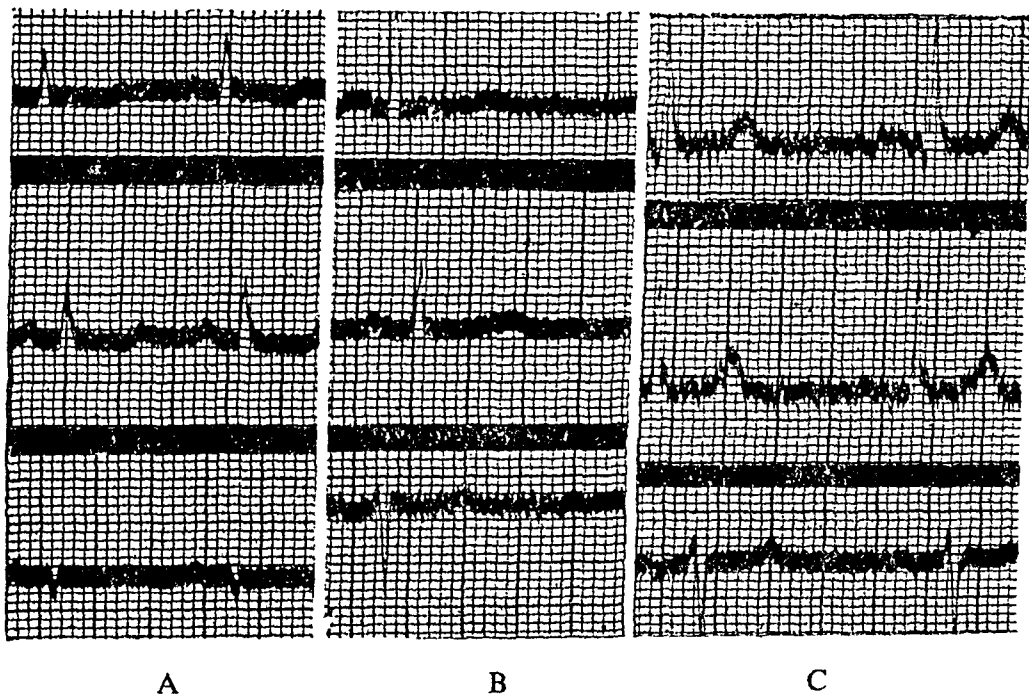
FIG. 3.—Electrocardiograms before and after treatment with vitamin B_1.

(A) December 6, 1939, before treatment; the QRS waves are of low voltage, the T waves are flattened and diphasic, and the P–R interval 0·12 sec.
(B) December 21, 1939, after 11 days' treatment; the QRS voltage is higher and the P–R interval is 0·16 sec.
(C) January 20, 1940, after further treatment; the voltage of the T waves is now increased as well as of QRS.

and T was upright in all leads. On January 20, 1940, there was further elevation of T in all leads (Fig. 3).

Estimation of Vitamin B_1 in the Urine.—This investigation was carried out by Dr. W. Kelly of the Royal Victoria Infirmary, Newcastle-upon-Tyne. Estimations were made of the vitamin B_1 content of twenty-four hour specimens of urine following a test dose of 2 mg. of vitamin B_1. The results, given below, show that no significant increase in the output of the vitamin occurred.

URINARY OUTPUT OF VITAMIN B₁ FOLLOWING A TEST DOSE

Day	Urinary Volume in c.c.	Urinary Content of Vitamin B₁ in thousandths of a milligram
1–2	700	106
2–3	760	29
3–4	1540	8
4–5	3500	10
5–6	2500	13
6–7	4600	17
7–8	4160	22

Test dose of 2 mg. of vitamin B_1 given at the start.

Dietary History

The patient's circumstances forced him to try to live on 9 shillings a week after he had paid his rent. Difficult enough in normal circumstances, the rise .of prices that followed the outbreak of war resulted in his already meagre diet dwindling progressively. His diet for the three months before admission is given below. It will be seen that the weekly intake of vitamin B_1 (819 international units) is far below the amount that is considered to be a minimal necessity. We are indebted to Dr. Margaret D. Wright, of the research staff of Vitamins, Hammersmith, for her trouble in estimating the vitamin B_1 content of this diet.

Usual Daily Diet	Weekly Total (including items that were taken once or twice in the week only)	International Units of Vitamin B_1
Breakfast.		
2 rounds of white bread	Bread, $4 \times 2\frac{1}{2}d.$ loaves	254
3 cups of tea with tinned milk	2 boiled eggs	50
	8 oz. tinned milk	95
	Potatoes $10\frac{1}{2}$ oz.	90
Dinner.	(twice)	
Kippers, fish cakes,	Sausage	100 (?)
black puddings, meat, or	Meat 1 lb.	230
sausage with potatoes	Beer $1\frac{1}{2}$ pints	0
		——
Tea.		819
2 rounds of white bread		
3 cups of tea with tinned milk		
Supper.		
None		

Discussion

This case appears to be one of pure dietary deficiency of Vitamin B_1. There was no excessive indulgence in alcohol, as in Jones and Bramwell's recent case (1939), and although no elaborate investigations were undertaken there is no reason to suspect gastro-intestinal disease, such as Ungley (1939) and many others have mentioned as a contributory factor. Furthermore the case presented no evidence of polyneuritis or skin pigmentation, as is described by Boyd Campbell and Allison (1940), but was a case of pure neart failure.

Summary

A case of beri-beri heart is recorded.

The deficiency was apparently due solely to defective diet.

A clinical cure followed the giving of vitamin B_1.

Electrocardiographic and radiological changes were present and disappeared after vitamin B_1 had been given to the patient.

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PULMONARY STENOSIS PRODUCED BY ANEURYSM OF THE ASCENDING AORTA

BY

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Although aneurysm of the aorta is not itself uncommon, its location so that pulmonary stenosis and insufficiency result and so that the symptoms and signs simulate those of aneurysm of the pulmonary artery justifies a report and brief discussion.

Case Report

A negro woman, 28 years of age, was first admitted to Charity Hospital of Louisiana at New Orleans in May 1938, complaining of shortness of breath, which had been present for two weeks. A month before, an attack of what she termed " indigestion " had been followed by severe diarrhœa with considerable tenesmus and the passage of pure blood; the diarrhœa disappeared within a week and she felt fairly well for two weeks. Then she had a sudden, severe stabbing pain in the left chest, radiating to the left shoulder. She was dyspnœic and restless. The pain continued, at first with remissions, until she entered the hospital. The past history contained no relevant facts.

Physical examination revealed a fairly well developed and well nourished woman who appeared acutely ill and was dyspnœic even on a high back rest. The pulse rate was 90 per minute, the respiratory rate 20, and the blood pressure 95/40. The skin and mucous membranes appeared slightly pale.

The chief physical findings were confined to the chest. There was slight fullness in the anterior thoracic wall in the third interspace, pressure over which elicited some pain. Expansion was equal on both sides, and resonance and breath sounds were normal. The apex beat of the heart was best seen and felt in the fifth interspace, slightly outside the mid-clavicular line. Percussion revealed the heart to be slightly enlarged to the left. There was a systolic thrill over the præcordium, and a continuous murmur with systolic accentuation, heard most clearly over the area of the pulmonary valve but also audible over the entire præcordium, and replacing the second pulmonary sound. The arteries felt normal and the pulse, although of slightly low tension, was otherwise normal and not of the Corrigan type.

The abdomen was somewhat distended, but was otherwise normal. Pelvic examination revealed old inflammatory disease and rectal examination showed external hæmorrhoids and lymphogranulomatous obstruction an inch from the

anal opening. The extremities were normal, and the reflexes were normal and equal on both sides. The urine was normal and the blood Wassermann reaction was strongly positive.

At this time, as on all subsequent admissions, the radiologist reported an aneurysm of the pulmonary artery (Figs. 1–2), the measurements of which were

A   B
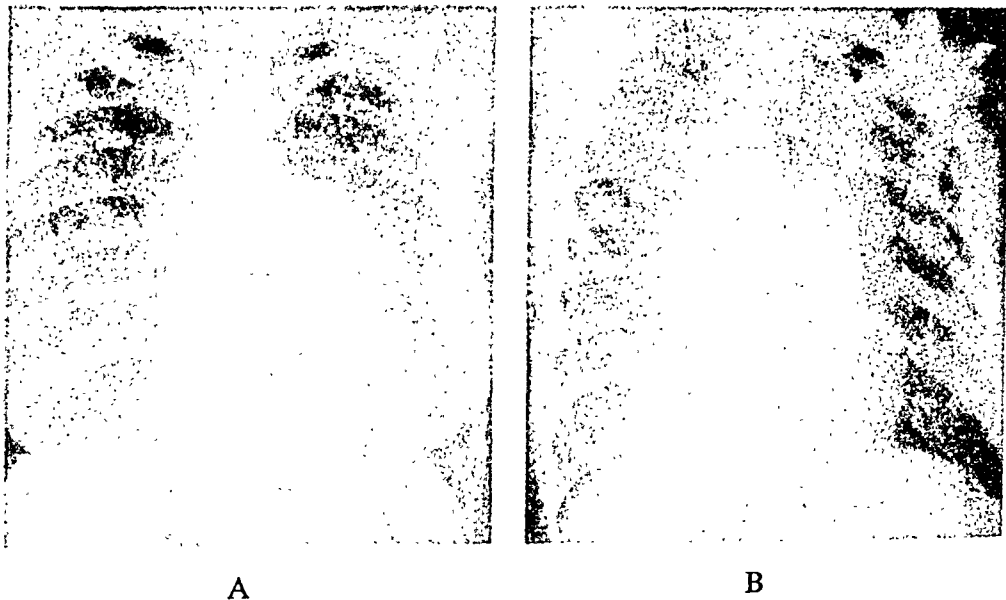
FIG. 1.—(A) Radiogram of chest, showing a normal aortic knob and enlargement in the region of the pulmonary conus and artery.
(B) First oblique position, showing the aneurysm of the ascending aorta.

A   B
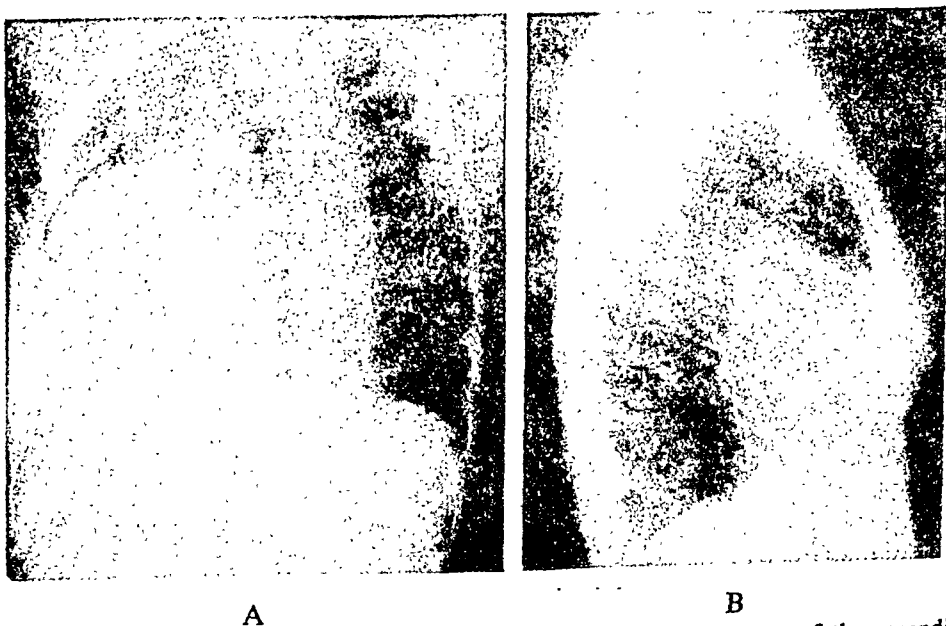
FIG. 2.—(A) Radiogram (second oblique position) showing the aneurysm of the ascending aorta.
(B) Lateral view of chest, showing the aneurysm of the ascending aorta pressing on the anterior thoracic wall.

never satisfactorily secured. The electrocardiographic report, which also was substantially the same on each admission, read as follows: very slight right axis deviation, P_1 and P_2 slightly high, P–R interval normal (0·16 sec.), Q–T slightly long (0·40 sec.), S–T slightly depressed, and T waves normal (Ashman's formula, 1939).

The patient discharged herself from hospital, but was readmitted later in the same month for treatment of her pelvic condition. She remained in a gynæcological ward for three weeks, the findings being essentially the same as those already recorded.

After a third admission in October for treatment of her rectal stricture, when she only remained in hospital five days, she was admitted for the fourth time in January 1939. She complained of the same stabbing pain in the chest, but it was now more severe. Her hands and feet had been swollen for some days.

The pulse rate was 88 per minute, the respiratory rate 18, and the blood pressure 130/78. She was dyspnœic, and the skin and mucous membranes were pale. Physical examination was essentially the same as before, except that tenderness in the præcordial area and the fullness in the third interspace were more pronounced. The continuous murmur with systolic accentuation was also more prominent. The liver was enlarged two fingers' breadth below the costal margin. There was no fluid in the abdomen, but there was a slight pitting œdema of the feet and ankles.

As during her first stay in hospital, the patient had slight daily rise of temperature to 99–99·5° F. Pain and dyspnœa continued, and symptomatic relief could be secured only by sedatives at regular intervals. She was unwilling to remain in hospital and was finally permitted to leave, unimproved.

She returned for the last time in March 1939, with all her symptoms and findings markedly exacerbated, and with clear evidence of congestive heart failure. She improved under treatment during the next two months, but developed pulmonary œdema in May and died within a few hours. Radioscopic examination shortly after she entered the hospital in March revealed the supposed aneurysm in the region of the pulmonary artery; at this time the posterior mediastinum was clear.

A post-mortem examination was made by Dr. Bjarne Pearson. Each of the pleural cavities contained 800 c.c. of straw-coloured fluid. The pericardial cavity was obliterated by fibrous adhesions, but it was fairly easy to separate the pericardium from the anterior surface of the heart.

The heart weighed 525 g. and had the following measurements: tricuspid valve, 13·0 cm.; pulmonary valve, 9·0 cm.; mitral valve, 10·0 cm.; aortic valve, 7·2 cm.; left ventricle, 2·0 cm.; right ventricle, 1·0 cm.; left auricle, 0·6 cm.; right auricle, 0·7 cm. The myocardium was firm and light red. No areas of infarction were seen. The coronary arteries showed no sclerosis and their orifices as well as their branches were normal.

The chief pathological finding was an aneurysm of the aorta, located above the junction of the right and left anterior cusps (Fig. 3). It formed a herniation that protruded into the pulmonary artery (Fig. 4), which in turn protruded into
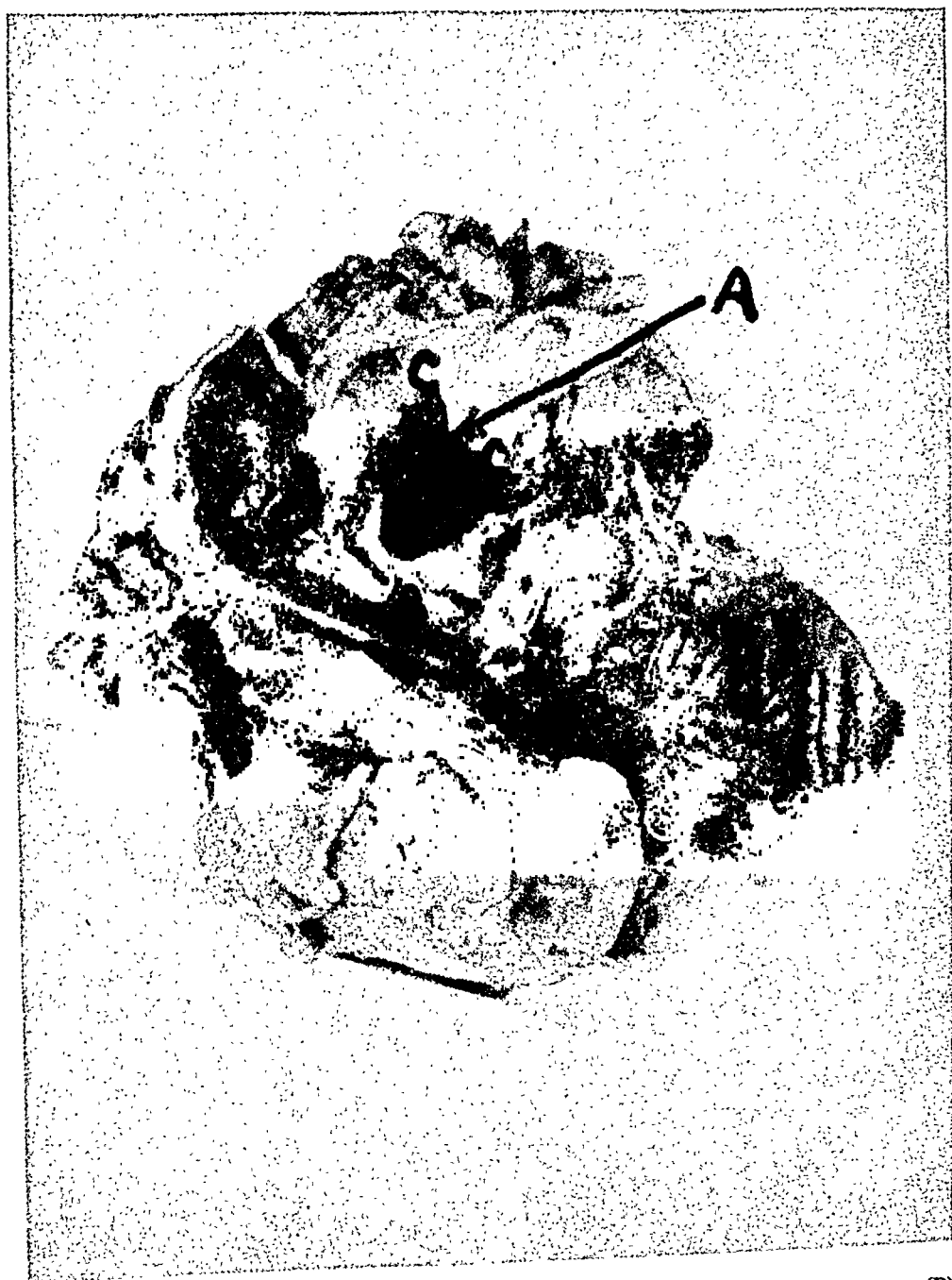
FIG. 3.—Heart, showing the aneurysm of the ascending aorta (A) above the aortic valves (B). The aneurysm extends between the origins of the coronary arteries, which are not well visualized. C indicates the area in the wall of the aneursym from which sections were taken for microscopic study.

FIG. 4.—Heart, showing aneurysmal sac (A) bulging into the pulmonary artery (B) and obliterating the left posterior cusp (C), thus producing pulmonary stenosis and insufficiency.   Note hypertrophy of right ventricle.

the right ventricle, the combined pressure and anatomical distortion causing stenosis of the pulmonary artery. The aneurysmal sac also distorted the right posterior cusp of the pulmonary valve so that it could not be recognized as such and appeared merely as a thin rim of tissue. Evidence of early pressure changes was seen on the internal surface of the chest overlying the aneurysm, but there was no erosion. The mouth of the aneurysm measured 2·25 by 2 cm., the depth was 5·75 cm., and the transverse and the posterior diameters were both 6·5 cm.

Except for the spleen, which weighed only 60 g., and the pelvic organs and rectum, which revealed the conditions described clinically, the other post-mortem findings were unimportant. Microscopic examination revealed syphilitic changes in the aorta.

The diagnosis was aneurysm of the aorta with pulmonary stenosis caused by herniation of the aneurysm into the pulmonary artery.

Comment

The pertinent literature is not extensive. Aneurysm of the pulmonary artery is rare. Wahl and Gard (1931) found only 70 cases on record up to 1925, including the case they themselves were reporting.

Crawford and de Veer (1932) reported an aortic aneurysm located 1 cm. above the right and left aortic valves, which pressed on the base of the pulmonary artery and conus, as well as on the interventricular septum, and thus produced a right bundle branch block. They cited the similar case reported by Rothschild *et al.* and the cases reported by Bruffalini and by Stejfa.

Delp and Maxwell (1938) reviewed the papers on rupture of aortic aneurysms into the pulmonary artery and collected 46 cases, including their own. They mentioned that Boyd had reported 18 such ruptures in 592 aortic aneurysms and Stevenson 3, and that single cases had been reported by Kappis, Peacock, Taylor, Kork, and Potter. Kampmeier (1938) found only one rupture into the pulmonary artery in 633 aortic aneurysms, and observed four aneurysms of the sinus of Valsalva in the same material.

As this paper was being prepared for press there appeared the report of Garvin and Siegel (1939) concerning three cases of cor pulmonale due to obstruction of the pulmonary artery by an aneurysm of the aorta. On the basis of their own and other observations they conclude that: if myocardial insufficiency, especially of the right heart, is evident; if radioscopy shows the aneurysm in such a position that it could press on the pulmonary artery; if the electrocardiogram reveals right axis deviation; and if all other causes of heart failure are excluded; then the diagnosis of obstruction of the pulmonary artery by pressure from an aortic aneurysm should be considered probable.

In the case here reported several clinicians were unable to agree upon the diagnosis, and aneurysm of the pulmonary artery, aneurysm of the aorta with rupture into the pulmonary artery, aneurysm of the sinus of Valsalva, and aneurysm of a patent ductus Botalli were variously suggested. The first was

considered the most probable, though the combination of an aneurysm of the pulmonary artery with a patent ductus Botalli was discussed as a possibility. The radiologists argued for an aneurysm of the pulmonary artery, because the films revealed a normal aortic knob with the main shadow overlying the region of the pulmonary artery (Figs. 1–2), and radioscopy shortly before death revealed a clear posterior mediastinum, which seemed to indicate that the aneurysm pointed forward in the region of the pulmonary artery. Wahl and Gard's views of pulmonary aneurysms are comparable with the views taken of this particular case.

Since the patient had previously been in fairly good health and had had no symptoms until her twenty-eighth year, the diagnosis of congenital heart disease as manifested by a patent ductus Botalli seemed somewhat unreasonable, particularly as the first complaint referable to the cardiovascular system was moderate dyspnœa, with stabbing pain in the præcordium. The continuous murmur heard over the chest, combined with the radiological findings, made the diagnosis of aneurysm almost a foregone conclusion. The præcordial pain as well as the extreme tenderness over the third left interspace favoured some involvement of the pulmonary artery. There was no evidence of mitral disease and the slight right axis deviation was considered due to some disease in the pulmonary artery itself. On the other hand, there was no doubt of the existence of an old syphilitic infection, as proved by repeated positive Wassermann reactions, and syphilis of the pulmonary artery is extremely rare. It was therefore felt that if the aneurysm did involve this artery, some cause other than syphilis must be responsible.

At autopsy these conflicting findings were made clear when the lesion was revealed to be an aneurysm of the aorta located immediately above the sinus of Valsalva and directed forward and slightly to the left. It pressed upon the base of the pulmonary artery and thus obliterated the posterior cusp and produced pulmonary stenosis and insufficiency.

Of the several reports on record concerning rupture of an aortic aneurysm into the pulmonary artery, the case reported by Crawford and deVeer (1932) resembles the case herewith reported so far as location is concerned. In this instance, however, rupture did not occur and the clinical picture simulated that of pulmonary aneurysm.

Summary

A case is reported in which an aneurysm of the aorta was so located as to produce pulmonary stenosis and insufficiency, and a clinical picture suggestive of aneurysm of the pulmonary artery. Previous reports are briefly reviewed, and it is pointed out that the location of the aneurysm in the reported case is very unusual, as are its ultimate effects upon the pulmonary system.

R

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ANEURYSMAL DILATATION OF THE PULMONARY ARTERY

BY

K. D. WILKINSON

Aneurysmal dilatation of the pulmonary artery as a result of congenital defect is most commonly associated with a patent inter-auricular septum. This was not so in the present case, which seems to be worth record on account of its rarity.

The child in question appeared normal up to the age of ten years. The second child of healthy parents, she had bronchopneumonia at the age of six and catarrhal jaundice at nine, yet no cardiac defect was noted ; at ten years of age she was a spare child who weighed 42 lb. She was then admitted (in March 1936) to the Children's Hospital in Birmingham on account of breathlessness. This had only been noticed a short time during the winter of 1935–36, and her mother had also observed that her heart beat unusually forcibly and that her chest bulged forward and to the left side.

She was a healthy-looking girl with a fresh colour, quiet and friendly, and not excitable. The respiratory movement of the chest on the left side was limited. The heart was considerably enlarged, the apex being difficult to localize accurately, but the maximum impulse lay in the seventh left interspace, four inches from the midline. The area of cardiac pulsation was extensive, and the cardiac dulness extended up into the second left interspace in the mid-clavicular line.

The pulse was regular, 120 per minute, and of poor volume. The blood pressure was 104/64 mm.

At the apex the first sound was loud and appeared to be double, with a long systolic murmur. The second sound was loud and sharp. At the base both sounds were loud and clearly heard, and the first was followed by a long, blowing systolic murmur, maximal in the second left interspace, but audible over a wide area. The second sound was loud and there was no diastolic murmur.

During her stay in hospital she improved and the pulse rate fell to under 90. The electrocardiogram showed a low voltage in lead I, with a tall R_2 and R_3 and a P–R interval of 0·16 of a second.

She was readmitted on April 29, 1939, because she had developed a spinal curvature—which was reported to be due to an early osteochondritis of the spine. She then weighed 50 lb. and had grown a good deal. The condition of the heart was as before: the systolic murmur was audible all over the chest;

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the second sound was remarkably loud everywhere; and there was no diastolic murmur. The sedimentation rate was 5, and there was no evidence of infection. Radioscopy confirmed the great enlargement of the heart and showed some dilatation of the right pulmonary artery and an enormous shadow coming from the left pulmonary root (Fig. 1). This was also well shown in a partial oblique view with the patient turned slightly to her left (Fig. 2).
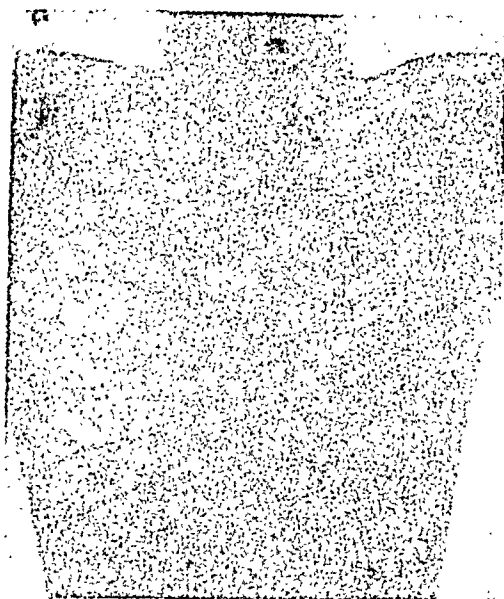
FIG. 1.—The direct antero-posterior radiogram (taken on April 14, 1939) shows gross enlargement of the pulmonary artery extending up to the second left interspace. The heart appears to lie a little to the left and the shadow almost completely fills the left chest. The pulmonary root on the right shows a large shadow, probably venous.

FIG. 2.—A slightly oblique radiogram, taken on April 14, 1939, shows the pulmonary distension and the cardiac enlargement below. The left lung is seen to be clear. The child had been slightly turned to the left, with the right shoulder forwards.

There had been no attack of syncope or cyanosis and no special complaint had been made about the heart. She was in hospital for a month and was provided with a spinal support, which she wore. After her discharge she continued to attend school, and appeared to enjoy normal health. She played no games and did not do physical exercises.

On September 5, 1939, when she came in from school at tea time, she said that she was tired and sat down. As she sat forward watching her mother transplanting a small plant, she suddenly put her hand to the left side of the chest and cried out " Oh, mother, the pain ! " She fell forward and was " dead in a minute."

Post-Mortem Findings

There was definite bulging of the thorax to the left and a slight degree of kypho-scoliosis. The pericardium was tremendously distended with fluid blood, and the heart so enlarged that the left lung was considerably compressed.

There were no pleural adhesions, but the left lung root was infiltrated with blood. The pulmonary artery was very large, the diameter being three inches, and its general appearance is well shown in Fig. 3. The effusion of clotted

FIG. 3.—Photograph of the heart and great vessels post mortem, showing the great dilatation of the pulmonary artery.

(A) Clot of effused blood between the aorta and the aneurysm of the pulmonary artery.
(B) Effused blood in the wall of the aneurysm.
(C) Left auricle.
(D) Opened right ventricle.

FIG. 4.—Photograph of the heart and great vessels post mortem.   The right ventricle and the
dilated pulmonary artery have been opened.

(A) Left pulmonary artery discoloured by effused blood.
(B) Effused blood in wall of dilated artery which has been opened.
(C) Site of rupture of the pulmonary artery.
(D) Two cusps of a bicuspid pulmonary valve.
(E) Just to the left of E is a small patency of the inter-ventricular septum.
(F) Tricuspid valve.

blood can be seen at A, between the aorta and the aneurysm of the pulmonary artery, and again at B, in the wall of the aneurysm (Fig. 3). The front of the artery and its left branch were infiltrated with blood extending into the root of the left lung.

About one inch above the valve was a linear split (Fig. 4 C), two inches in length, extending through the intimal coat and the medial coat and at one point through to the pericardium ; elsewhere the adventitial coat remained thin film like tissue-paper.

Above the split the wall of the artery was dissected between the media and adventitia well into the root of the left lung, and this is shown in Fig. 4 (A and B).

Both the ventricles were somewhat enlarged, and their walls were thickened, while immediately below the pulmonary orifice was a small inter-ventricular communication (Fig. 4 E). The aorta was possibly slightly smaller than normal for the age.

The pulmonary valve was bicuspid and very large (Fig. 4 D), the cusps being quite soft and of normal texture. The aortic, mitral, and tricuspid valves were normal.

The auricles were not noticeably abnormal and the inter-auricular septum was intact. The myocardium appeared normal.

Summary

A case is reported in which an aneurysmal dilatation of the pulmonary artery, due to a congenital defect, led to sudden death from rupture of the walls of the artery, the rupture also producing some degree of dissection of the coats of the artery.

A NOTE ON PULSATING MANUBRIAL TUMOUR

BY

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From University College Hospital

Received June 22, 1940

In the two cases that are here described pulsating tumours over the upper part of the sternum simulated pointing aneurysms, but were in reality secondary deposits from neoplasms elsewhere.

Case 1

In December 1932 a man of 48 was sent to me for an opinion. He said that 15 months previously, while engaged in work as a house demolisher, he fell down two stories through a shaft. He broke an arm, a leg, and ribs, and had been unable to work since the accident. His chief complaints were of shortness of breath and of pain over the region of the upper part of the sternum, radiating to the shoulder and down the arms to the elbows, though unrelated to exercise. He came diagnosed as a case of aneurysm of the aorta, and a second opinion was required because he was claiming compensation for injury arising out of his employment. On stripping him I found an obvious swelling over the manubrium sterni. It extended from the top of the manubrium to the upper border of the first rib, and a little beyond the sides of the sternum laterally. The rounded lump projected about 1·5 cm. ; the skin over it was not discoloured ; there was visible and palpable pulsation, the tumour expanding with each heart beat. A long but inconspicuous systolic murmur was audible over the tumour. The Wassermann reaction was positive. The pulses were equal, and there were no pressure symptoms or signs. At first there seemed little reason to question the diagnosis, but closer examination gave rise to increasing doubt. The first point to arouse suspicion was the shape of the tumour itself ; in the middle line the mass was hemispherical, but in the first right interspace an inconspicuous flattened tongue projected from it for 2 cm., also pulsating. Moreover, a finger could be carried down behind the sternum a little way without meeting resistance. The second point was that the pulsation of the tumour, when compared with that of the carotid artery, seemed softer and less abrupt than was to be expected, and very slightly but distinctly delayed. He gave incidentally a history of passing a small quantity of blood in the urine on two occasions many months before. The urine was normal, but the blood urea was a little raised. The right kidney was palpable and seemed enlarged. I refused to confirm the diagnosis of aneurysm, believing the tumour to be a new growth.

I was asked to re-examine the man in March 1934, 15 months later, from the same point of view as previously.   His symptoms were unchanged ; so were the signs, except that the manubrial tumour had increased perceptibly in size, and he was thinner.   On this occasion, however, X-ray examination detected what was not present before, namely, an abnormal shadow above the level of the knob of the aorta, extending also above the level of the manubrium, and a clear picture of a secondary deposit in the upper part of the shaft of the left humerus.

The diagnosis was now unmistakably hypernephroma with secondary deposits.

The interest of the case lay, of course, in its original resemblance to pointing aneurysm, and most noteworthy were the relative softness of the pulsation and the slight but perceptible delay in its rise, a delay confirmed at the time by records shown in the figure below.
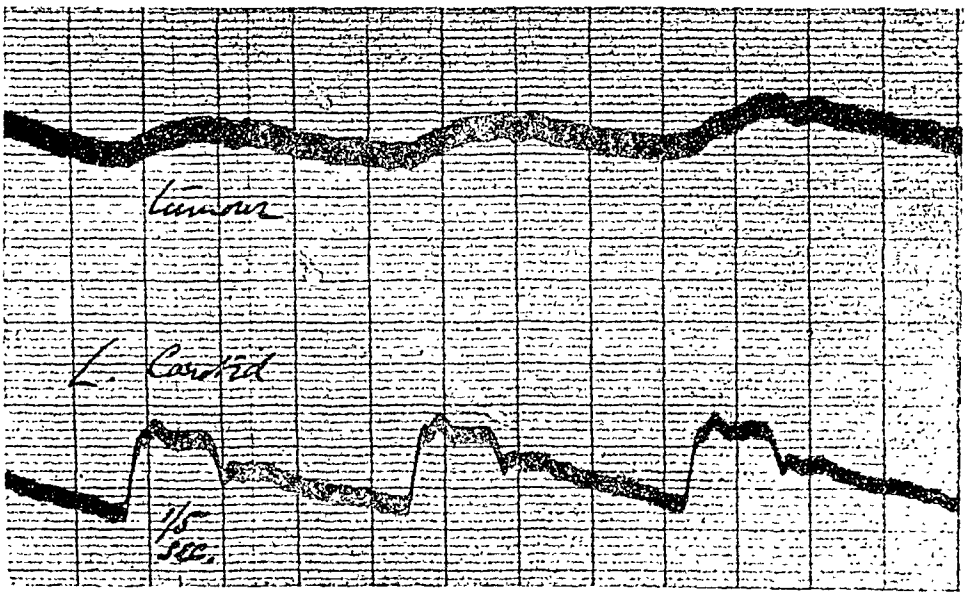
FIG. 1.—The upper curve, taken from over the tumour in the manubrium sterni, indicates that pulsation there was slightly later than the pulsation of the carotid pulse.

Case 2

In June 1939 a man of 58 years was admitted under my care complaining of hiccough and vomiting of six weeks' duration, the passage of a little blood in the urine for three weeks, and a lump that had developed recently over the upper part of the chest.

He had full signs of tabes dorsalis and a tongue presenting advanced chronic superficial glossitis ; the Wassermann reaction was positive.

A tumour projected over the right sterno-clavicular joint and below it.   It was hemispherical, and about 5 cm. in diameter, and pulsated quite distinctly. The heart was much enlarged, and over the tumour a loud systolic murmur was audible.   The second right space was dull to percussion, and a tracheal tug was

detected ; the pulses and pupils were equal, and there were no pressure signs. X-ray examination showed a greatly dilated aorta. The blood pressure was 220 systolic, 140 diastolic; the blood urea shortly rose from 130 mg. to 270 mg. within a few days, and the man died uræmic. During life the kidneys were not felt, but albumin and occasional red cells were found in the urine.

In demonstrating this patient I remarked upon the unusual softness and slow rise of the pulsation in the tumour, and recalled and summarized the case of hypernephroma previously seen and here described as Case 1. But because this patient had a clear X-ray picture of an enlarged aorta and a tracheal tug, a diagnosis of aneurysm pointing through the chest wall seemed unavoidable, the urinary symptoms being ascribed to renal sclerosis and insufficiency.

At autopsy the heart was found greatly enlarged, the pericardium completely obliterated by old adhesions. The aortic valves were very atheromatous and a little incompetent. The aorta was greatly dilated, and its wall presented gross syphilitic changes. But there was no aneurysmal projection through the sterno-clavicular joint, which was occupied by a deposit of new growth, spreading from the manubrium sterni and secondary to a large hypernephroma of the upper pole of the right kidney. The left kidney was granular on the surface and very fibrotic on section.

Summary

Two cases are briefly described in which pulsating tumours over the upper part of the sternum in syphilitic subjects seemed to indicate pointing aneurysm. Both tumours were in fact secondary deposits from hypernephroma, though in one case aneurysmal dilatation of the aorta was present as well. The cases are of interest in emphasizing softness and slowness and a slight but just distinct delay in the rise of the pulse in these pulsating neoplasms.

ŒSOPHAGEAL ELECTROCARDIOGRAMS IN AURICULAR FIBRILLATION *

BY

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A critical study of electrical events occurring in the posterior portions of the human heart has been made possible by the use of œsophageal leads in clinical electrocardiography (Cremer, 1906; Lieberson and Liberson, 1934; Luisada, 1935; Brown, 1936*a*, 1936*b*; Hamilton and Nyboer, 1938; Spühler, 1938; Nyboer, 1939; Deglaude and Laubry, 1939). The œsophagus lies close to the posterior surface of the left auricle, being separated from it by a space, 0·5–1 cm. wide, composed of areolar tissue and by the two layers of the pericadium. The right auricle lies 4–6 cm. anteriorly, across the cavity of the left; but beneath the most inferior part of the left auricle the œsophagus is separated from the inferior vena cava and the right auricle by a distance of only 1–2 cm.

Brown (1936*a*) showed that an electrode lying in this part of the œsophagus provided a nearly direct lead for the surface of the left auricle and, when paired with a distant electrode, was capable of recording faithfully the electrical changes of this region. From his study of 21 patients exhibiting auricular fibrillation Brown (1936*b*) concluded that, when it has become established and is not liable to spontaneous reversion to normal rhythm, the auricular deflections recorded by the œsophageal lead are of small amplitude and irregular form and do not exhibit intrinsic deflections, although the electrode lies against or close to the posterior (left auricular) segment of the pathway round which a circulating mother impulse is supposed to travel. Deglaude and Laubry (1939) also failed to record intrinsic deflections. Brown, however, did obtain records showing intrinsic deflections from two patients in whom fibrillation was associated with thyrotoxicosis; in one of these normal rhythm appeared after thyroidectomy. He suggested that, when auricular intrinsic deflections are recordable by the œsophageal lead, fibrillation may not be firmly established and may be susceptible to spontaneous reversion.

We decided therefore to examine by means of the œsophageal lead cases of auricular fibrillation in which the arrhythmia was known to be paroxysmal or

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* The results of this study were presented in abstract before the Edinburgh Pathological Club in March, 1939.

those in which normal rhythm was restored by quinidine, and to compare the resulting curves with those obtained from cases of established fibrillation.

The method employed, modified from that of Brown, has been described (Hamilton and Nyboer, 1938). Records were obtained in each case from several auricular levels as well as from supra- and infra-auricular sites. Repeat œsophageal cardiograms were always made from the same levels as the original records except where otherwise stated in the figures.*

Nine patients exhibiting auricular fibrillation were studied. Reversion to normal rhythm occurred in four, quinidine having been given to three of these, and in the other five fibrillation persisted.

I. Cases that Reverted to Normal Rhythm

In all four the auricular deflections recorded by the œsophageal lead were of greater amplitude than those in the standard lead tracings.

Three cases where auricular intrinsic deflections were recorded

Case 1 was that of a female, aged 35, suffering from chronic rheumatic mitral disease: she had had short attacks of dyspnœa for fifteen years, paroxysmal fibrillation having been recorded several times during the previous three years. Digitalis was given for the relief of congestive cardiac failure, but no quinidine.

Cardiograms (Fig. 1 B) by standard leads showed auricular fibrillation with coarse " f " waves having a maximum amplitude of 0·3 mv. In the œsophageal cardiograms † numerous auricular intrinsic deflections were seen, often in pairs or groups separated by smaller, irregular, slurred waves. A normal curve is shown for comparison in Fig. 1 A. The maximum amplitude of the auricular deflections was 0·6 mv. and the minimum less than 0·1 mv. After reversion to sinus rhythm normal œsophageal curves were obtained.

Case 2 was that of a male, aged 48 years, suffering from coronary arterial disease and chronic alcoholism. Fibrillation started two weeks before admission with sudden palpitation, dyspnœa, and œdema which was not relieved by full digitalization; salyrgan, however, caused marked diuresis and the patient lost 43 lb. of weight in seven days with clinical improvement. Fibrillation was still present five weeks later. Normal rhythm was restored when 1·0 g. of quinidine sulphate had been taken in two days, and remained for a further six months during which he took no quinidine.

Standard lead cardiograms (Fig. 1 C), made before quinidine was given, showed fibrillation with low voltage " f " waves having a maximum amplitude of 0·2 mv. Œsophageal cardiograms contained many auricular intrinsic deflect-

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* Since the work recorded in this paper was carried out the joint recommendations of the American Heart Association and the Cardiac Society of Great Britain and Ireland relating to the method of recording præcordial and other semi-direct leads have been generally accepted. We have therefore reversed all œsophageal lead curves in this paper so that they conform in appearance to those which may be obtained by the new method of leading.

† In this and all subsequent descriptions the term " œsophageal cardiogram " is used to refer to the tracing obtained when the electrode lay at the level of the auricles. The ventricular œsophageal electrocardiogram is not considered in this paper.
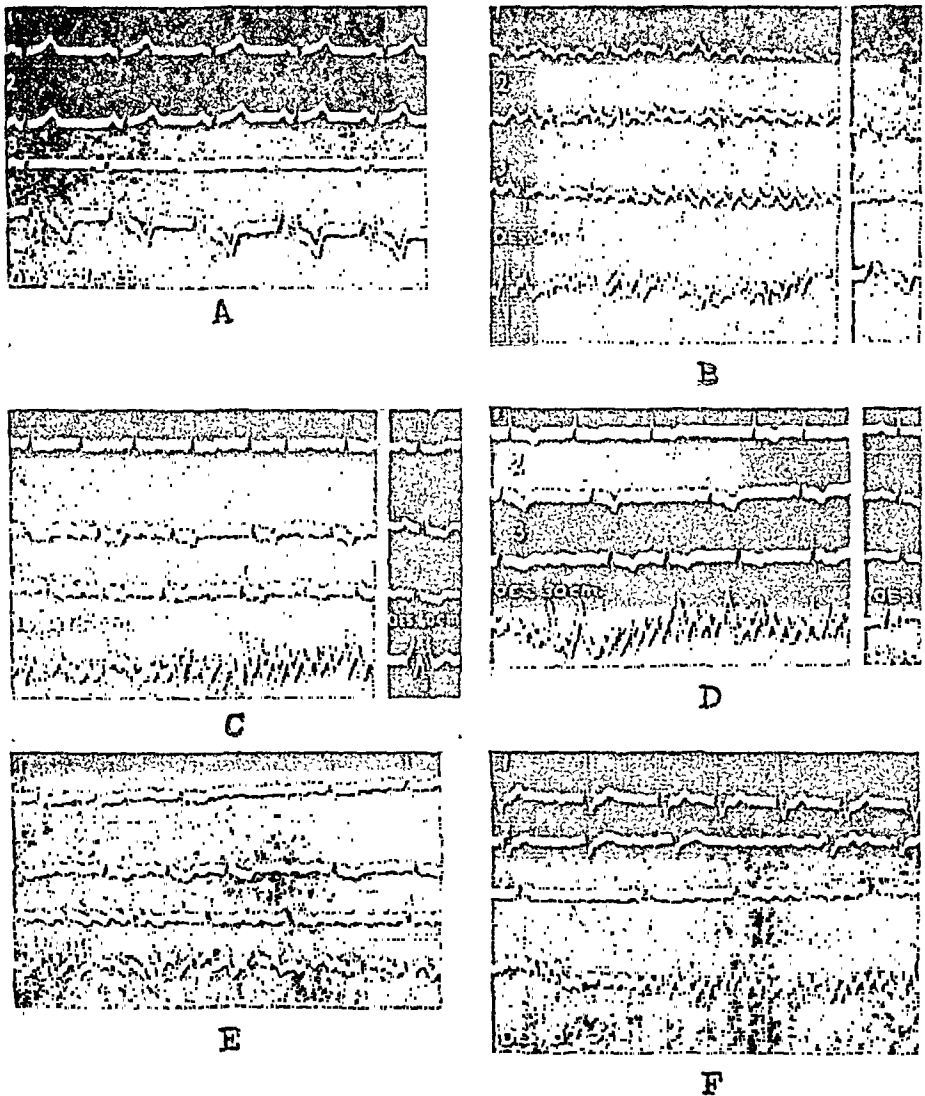
FIG. 1.—(A): Standard and œsophageal lead cardiograms of a normal male, aged 30 years, for comparison. In this and the other figures the distance of the mid-point of the œsophageal electrode from the incisor teeth is recorded. String sensitivity, 1 mv.=10 mm. Time-marker, 0·2 and 0·04 second.

(B)–(E): Auricular intrinsic deflections in œsophageal cardiograms.

(B) Case 1; (C) Case 2 ; (D) Case 3: auricular fibrillation; subsequent normal rhythm.

(E) Case 5, (F) Case 6: auricular fibrillation; no return of normal rhythm.

ions; they occurred in groups separated by smaller, irregular, slurred waves, and had a maximum amplitude of 0·8 mv. and a minimum of less than 0·1 mv. After normal rhythm was restored they were of normal form.

Case 3 was that of a male, aged 53, suffering from arteriosclerosis and coronary arterial disease; he had complained of dyspnœa on exertion for one year. Rhythm was normal, apart from occasional supraventricular extrasystoles, until the tenth day after admission, when the auricles started to flutter at a rate of 300 per minute with a 2 : 1 A-V ratio. Fibrillation was induced by

digitalis and persisted for ten days, after which quinidine sulphate was given along with the digitalis; after 1·8 g. had been taken in two days normal rhythm reappeared and remained.

Fibrillation with small "f" waves, having a maximum amplitude of less than 0·1 mv., was shown in the standard lead cardiograms (Fig. 1 D) taken before quinidine was given. In the œsophageal cardiograms numerous auricular intrinsic deflections were seen, occurring in groups separated by smaller, irregular, slurred waves; they had a maximum amplitude of 0·7 mv. and a minimum of 0·2 mv.; after the reappearance of normal rhythm they were of normal form.

One case where no auricular intrinsic deflections were recorded

Case 4 was that of a male, aged 56, suffering from arteriosclerosis and coronary disease. Paroxysms of fibrillation had been recorded repeatedly during the preceding four years, and had usually ceased spontaneously though digitalis had often been given. The paroxysm observed by us lasted for two days and ended after 0·2 g. of quinidine sulphate; no digitalis had been given.

During the paroxysm standard lead cardiograms (Fig. 2 A, see page 267) showed fibrillation with small "f" waves having a maximum amplitude of 0·1 mv. In the œsophageal cardiograms the auricular deflections were very irregular in size and form, being only slightly larger than the "f" waves of the standard lead curves. Although many feet of record, obtained from various auricular levels, were studied, no certain instance of intrinsic deflection could be found. The auricular deflections had a maximum amplitude of 0·3 mv. and a minimum of 0·1 mv. Normal œsophageal curves were secured after normal rhythm reappeared.

II. CASES THAT DID NOT REVERT TO NORMAL RHYTHM

In all five the auricular deflections recorded by the œsophageal lead were of greater amplitude than those in the standard lead tracings.

Two cases where auricular intrinsic deflections were recorded

Case 5 was that of a female, aged 46, suffering from chronic rheumatic mitral disease and an acute exacerbation. She had had dyspnœa on exertion for six years. The presence of fibrillation had been recorded ten weeks before the observed hospital period during which the arrhythmia was continuously present. She received digitalis but no quinidine.

Standard lead cardiograms (Fig. 1 E, see page 265) showed fibrillation with " f " waves of moderate size having a maximum amplitude of 0·2 mv. In the œsophageal cardiograms the auricular complexes were of varying amplitude, some smaller and some larger than those in the standard lead curves. A few auricular intrinsic deflections were recorded, but these tended to occur singly and were separated by completely slurred waves; the maximum amplitude was 0·5 mv. and the minimum less than 0·1 mv.

Case 6 was that of a male, aged 79, suffering from arteriosclerosis and coronary disease. He had had increasing dyspnœa on exertion for one year

and œdema of the ankles for five weeks. There was no definite episode suggesting the onset of the auricular fibrillation, which remained throughout his 18 days in hospital. He received digitalis but no quinidine.

Standard lead cardiograms (Fig. 1 F) showed auricular fibrillation with small " f " waves having a maximum amplitude of 0·1 mv. In the œsophageal curves numerous auricular intrinsic deflections were seen, occurring in groups between which were smaller, irregular, slurred waves; they had a maximum amplitude of 0·45 mv. and a minimum of less than 0·1 mv.

Three cases where no auricular intrinsic deflections were recorded

Case 7 was that of a male, aged 76, suffering from arteriosclerosis and coronary disease, who had complained of dyspnœa on exertion and œdema of the ankles for two years. Throughout this period auricular fibrillation was known to be present. He was given digitalis but no quinidine.

Standard lead cardiograms (Fig. 2 B) showed fibrillation with small, often imperceptible " f " waves having a maximum amplitude of less than 0·1 mv. In the œsophageal tracings the auricular waves were also small, though larger than those in the standard lead curves, having a maximum amplitude of slightly over 0·1 mv. Although records were made from many auricular levels no auricular intrinsic deflections were seen.

Case 8 was that of a male, aged 69, suffering from coronary disease and hypertension, with congestive cardiac failure in varying degree for three years.
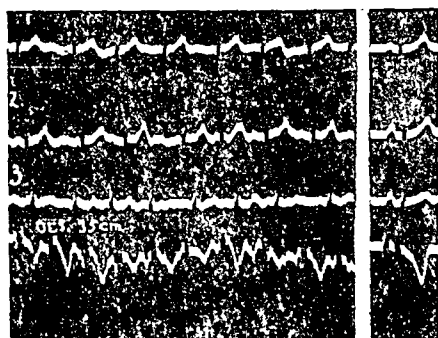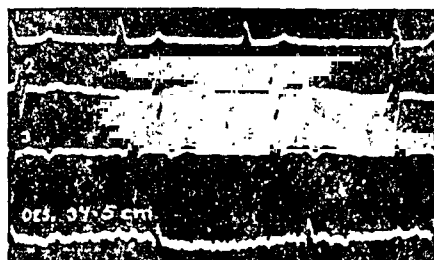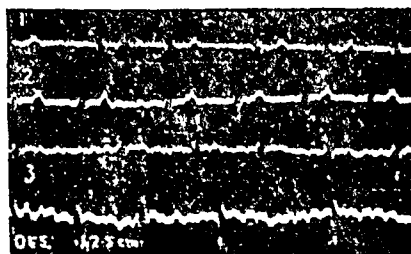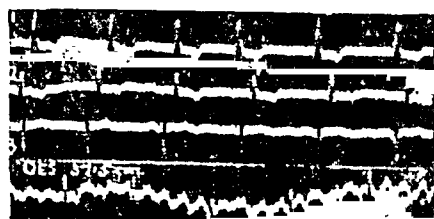
FIG. 2.—No auricular intrinsic deflections in the œsophageal cardiogram.

(A) Case 4: auricular fibrillation: subsequent normal rhythm.
(B) Case 7, (C) Case 8, (D) Case 9: auricular fibrillation: no return of normal rhythm.

Normal rhythm had been present two years before. Three weeks before admission he had a sudden increase in breathlessness and œdema, possibly indicating the onset of fibrillation, which was present on admission and remained. He was treated with digitalis, but was not given quinidine.

Standard lead cardiograms (Fig. 2 C), showed fibrillation with very small " f " waves having a maximum amplitude of less than 0·1 mv. Although œsophageal tracings were made from several auricular levels no auricular intrinsic deflections were seen; the auricular waves had a maximum amplitude of 0·2 mv. and a minimum of less than 0·1 mv.

Case 9 was that of a male, aged 60, suffering from hypertension. He was admitted with dyspnœa and œdema of the ankles of two weeks' duration. Auricular fibrillation was recorded several times during the first month when symptoms were severe, but normal rhythm appeared later as he improved under digitalis and salyrgan therapy. He remained well for three months after discharge, when dyspnœa and œdema suddenly returned; he was then readmitted. Although improvement again followed similar treatment, fibrillation was present throughout his three weeks in hospital. He received no quinidine.

Standard lead cardiograms (Fig. 2 D), taken during the second admission, showed fibrillation with very small " f " waves having a maximum amplitude of less than 0·1 mv. The auricular deflections in the œsophageal cardiograms, also taken at this time, were of moderate size having a maximum amplitude of 0·25 mv. and a minimum of less than 0·1 mv., but, although several auricular levels were examined, no auricular intrinsic deflections were recorded.

DISCUSSION

Since we have recorded auricular intrinsic deflections by the œsophageal lead in five out of nine cases of auricular fibrillation, it would appear that such deflections are more frequently present in œsophageal cardiograms in this arrhythmia than has been supposed. The present work fails to support Brown's contention (1936b) that they are to be found only in cases liable to spontaneous reversion to normal rhythm. They were found in one case of paroxysmal fibrillation (Case 1), and in two of fibrillation of recent onset, responding to quinidine (Cases 2 and 3), but also in one case of fibrillation and rheumatic heart disease with a six years' history of congestive failure (Case 5), and in one case of fibrillation and coronary disease with a year's history of congestive failure (Case 6); in the last two auricular fibrillation might be expected to remain established.

On the other hand, auricular intrinsic deflections were not recorded in one case of paroxysmal fibrillation (Case 4), in one case in which normal rhythm had been present five months before (Case 9), in another in which normal rhythm had been recorded two years before and in which fibrillation may have been present for only three weeks prior to admission (Case 8), and in a fourth in which fibrillation was known to have been present for two years before admission (Case 7).

The presence or absence of auricular intrinsic deflections in the œsophageal lead tracings of cases of fibrillation does not indicate the likelihood or otherwise of reversion to normal rhythm, for, of the four instances of such reversion, one

(Case 4) showed no intrinsic deflections although the fibrillation was paroxysmal, and, of the five cases in whom the arrhythmia persisted, two (Cases 5 and 6) did show intrinsic deflections.

The work of Garrey (1914, 1924) and of Brams and Katz (1931) has produced evidence that, in experimental animals, induced auricular or ventricular fibrillation is not necessarily associated with the development of a circus movement of the impulse or of control of the activation of the muscle by a central circulating mother wave. Brown (1936b) analysed two simultaneous tracings taken by œsophageal leads in a case of auricular fibrillation and came to the conclusion that no central circulating wave was present in the auricles; no intrinsic deflections were seen in these records. It seems reasonable to suppose, from the records published by Brown and by Deglaude and Laubry, as well as from our own, that in many cases auricular intrinsic deflections are not obtainable. In these, therefore, there is no sign that co-ordinated activation of large muscle masses takes place, at any rate in the posterior part of the left auricle, such as would be expected if a central mother circus wave existed.

On the other hand, our records show that there are cases of fibrillation in which many auricular intrinsic deflections can be recorded. In these simultaneous activation of large muscle masses lying close to the electrode occurs frequently. The repetition of the deflections suggests the repetition of the same electrical process and is compatible with a central circulating impulse.

Brown's study (1936b) of œsophageal cardiograms in auricular flutter provides valuable evidence in support of the theory of Lewis and his associates (1921, 1925) that this arrhythmia is due to the continual circulation of an impulse round a more or less constant path. Brown's published and our unpublished œsophageal lead curves of flutter and the direct lead curves of experimental flutter published by Lewis (1921) show a close resemblance in the form of the auricular complexes to those obtained by us in auricular fibrillation (see especially Case 3, Fig. 1 D); this is striking enough to suggest that a similar mechanism is involved. However, two differences are apparent, namely, that in fibrillation the auricular rate is higher than in flutter (in our cases from about 375 to 500 per minute), and that in fibrillation the intrinsic deflections occur in groups separated by irregular smaller waves, whereas in flutter there is a constant wave-form. Sometimes, as in Case 5, intrinsic deflections are sparse, occurring singly. If the similarity between the auricular complexes in flutter and the complexes in fibrillation with intrinsic deflections can be considered to show that a circus movement exists in the latter, it must be argued that the path of the circus varies. When intrinsic deflections are recorded the circus must have passed close to the electrode but when the auricular complexes are small, irregular, and slurred, the path of the circus must have moved away from the proximity of the electrode, and the muscle near the electrode must have been irregularly activated in small masses by offshoots some distance from the central circus. A gradual change from complexes showing intrinsic deflections to slurred complexes without intrinsic deflections, suggestive of a gradual movement of the path of the circus away from the proximity of the electrode, is shown in Fig. 1 F (Case 6).

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In the cases not showing intrinsic deflections long records were taken from various auricular levels. Since the œsophageal lead is capable of recording such deflections if long enough records are taken, it is probable that no mechanism involving the simultaneous activation of large muscle masses in the posterior wall of the left auricle or in the wall of the right auricle immediately medial to the entrance of the inferior vena cava was at work in these instances. In these cases the arrhythmia is unlikely to have been associated with a single circulating mother impulse.

Garrey (1924) stated that in experimental flutter and fibrillation there might be any degree of " circus movement " from a large-ring central mother circus in flutter to delirious fibrillation with many small ring-like circuits varying in location according to changes in the degree and position of local areas of block. The results of this study suggest that this hypothesis may be extended to human auricular fibrillation. At the one end of the scale are those in whose œsophageal cardiograms numerous intrinsic deflections occur, giving the tracings an appearance closely resembling those of auricular flutter. At the other end are those where the auricular deflections are small and irregular without any intrinsic waves.

SUMMARY

1. Nine cases of auricular fibrillation have been examined by means of the œsophageal lead; in four a return to normal rhythm was observed.

2. Auricular intrinsic deflections were obtained in five cases, one of paroxysmal fibrillation, two of recent fibrillation responding to quinidine, and two in which the arrhythmia remained established.

3. Auricular intrinsic deflections were not found in the remaining four cases, one of paroxysmal and three of established fibrillation.

4. No association was found between the presence of auricular intrinsic deflections in the œsophageal cardiograms of the patients studied and the likelihood of reversion to normal rhythm.

5. The mechanism of auricular fibrillation is discussed in the light of the curves obtained.

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MYOCARDIAL AND PERICARDIAL LESIONS DUE TO NON-PENETRATING INJURY

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Subacute and chronic affections of the myocardium due to non-penetrating injuries have in the past been regarded as extremely rare. Traumatic rupture of the cardiac valves, papillary muscles, and chordæ tendinæ are described in detail in most textbooks; yet isolated myocardial and pericardial lesions, though undoubtedly more common, are scarcely mentioned except in more recent manuals dealing with diseases due to trauma, such as those by Stern (1930), Brady and Kahn (1937), and Spicer (1939). Papers by Beck (1935) and by Bright and Beck (1935) have dealt especially with such cardiac muscle injuries.

In my monograph (Warburg, 1938) I analysed 189 collected cases of traumatic heart disease, 158 of which seemed well substantiated, and added 13 new cases. This covered the long period from 1676, when Oluff Borch observed the first case, to the end of 1937. To these 202 cases analysed in 1938, I can now add 54 published cases previously overlooked and 5 new unpublished cases, making 261 in all. After excluding some of the earlier ones as doubtful, there remain 225 well-substantiated cases to form the basis of this review. One third of these have been published during the last five years.

The 59 new cases, not included in my previous study, are as follows: Bricheteau (1844), Steiger (1864), Müller (1879), Barth and Roger (1880), Reynier (1880) two cases, Barber (1912), Fraenkel (1917), Krumbhaar and Crowell (1925), Coffen (1930), Meixner (1931) four cases, E. E. Davis (1931), N. S. Davis (1931) two cases, Jervell (1933), Gunewardene (1934), Hawkes (1935), Kampmann (1935), Schilder (1935), Bean (1937) three cases, Kissane (1937) nine cases, Barber (1938) ten cases, Kienle (1938), Moritz and Atkins (1938), Peters (1938) two cases, Störmer (1938), Campbell (1939), O'Farrell (1939), Smith and McKeown (1939), Rajasingham (1939), Wüllenweber (1939), and five unpublished cases observed by or communicated to me.

PERICARDITIS

Blunt injuries to the heart must often cause pericardial hæmorrhage or fibrinous exudation. In the previous material of 202 cases, involvement of the

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pericardium was mentioned in at least 50, and in the new material in 10 cases, but I believe that pericardial lesions are actually far more frequent than is indicated by these figures.   The diagnosis usually rests on pericardial friction sounds, but sometimes characteristic splashing sounds have been heard (*bruit de moulin*, *bruit de rou hydraulique*), indicating pneumopericardium; four such cases were found in my first series and I have since discovered six more, summarized below.

(1) *Bricheteau (1844)*.—A shoemaker, aged 59, was hit in the chest by a waggon shaft, after which he suffered from pain in the chest for some years.   His wife could hear a gurgling sound in his chest.   He was admitted to hospital with cardiac failure ; tympany over the præcordium and a *bruit de moulin* were observed.   He died within a few days and post-mortem showed fibrinous deposit over the pericardium, which contained 250 c.c. of sero-purulent fluid and much air.

(2) *Steiger (1864)*.—A rural worker, aged 35, fell down 26 steps and hurt the left side of his chest against the frozen ground, causing a fracture of the left radius and injury to the left shoulder.   Severe pain and dyspnœa followed, and two hours after the accident a splashing sound or *bruit de moulin* was audible at a distance from the chest.   In the horizontal posture the cardiac dulness had disappeared.   His ribs may have been fractured, but there was no hæmoptysis and no evidence of pneumothorax. After some days the splashing sound disappeared and pericardial friction developed. The patient recovered completely.

(3) *Müller (1879)*.—A stone-cutter, aged 28, was crushed between two large stone flags, fracturing both clavicles and the left fifth and sixth ribs.   He became breathless, the pulse accelerated, subcutaneous emphysema of the left chest wall appeared, and pericardial and pleural friction sounds were heard.   Soon the cardiac dulness disappeared and the *bruit de moulin* was audible, ceasing in three weeks' time, when pericardial friction reappeared.   After a period of fever the patient recovered completely, and left hospital ten weeks after the accident.

(4) *Barth and Roger (1880)*.—A man, who three months previously had a fainting fit, fell down 12 metres and fractured both his arms.   Tympanitic percussion note was found over the heart and a definite *bruit de moulin* ; five months after the accident he had recovered.

(5) *Reynier (1880)*.—A man fell down 5 metres and lost consciousness.   He hurt his left side and felt severe pain in his left flank, where subcutaneous emphysema was found, reaching the præcordium.   The fourth, fifth, and sixth left ribs were fractured. The *bruit de moulin* was heard with the patient lying, but disappeared when he sat up ; it lasted only 24 hours.   No signs of pneumothorax.   The patient seems to have recovered completely.

(6) *Reynier (1880)*.—A man, aged 23, was crushed between the buffers of two railway carriages.   He did not lose consciousness, there was no hæmoptysis, and shock was slight.   He seemed to have fractured his fifth, sixth, and seventh left ribs. The *bruit de moulin* was heard and the cardiac dulness disappeared.   One month afterwards he was discharged apparently cured.

Meixner (1931) has recorded a case of traumatic pericarditis with effusion in which 300 c.c. of clear fluid were aspirated, and Rajasingham (1939) another case in which 175 c.c. of hæmorrhagic pericardial fluid were removed ; both patients recovered.   Paracentesis of the pericardium has, however, seldom been necessary, and in my previous paper there was only one case (Moullin, 1897) in which a large amount of fluid was removed by pericardiotomy.   Characteristic cardiographic changes in a case of traumatic pericarditis have also been described (Smith and McKeown, 1939).

The prognosis in traumatic pericardial lesions that are not complicated by extensive myocardial damage or by infection is benign. I have only found four fatal cases in which myocardial lesions were not present post-mortem, and these were described so briefly that myocardial damage cannot quite be excluded. Three or four cases developed pyogenic pericarditis and in several the injury was followed by tuberculous pericarditis. Finally, intrapericardial adhesions have been observed and in one case a constriction syndrome developed (Warburg, 1933).

AURICULO-VENTRICULAR BLOCK

My previous paper included 6 published cases of A-V block; in 3 the block was transient (Howat, 1920; Rosenson, 1924; Touhy and Boman, 1931) and in 3 it was permanent (Laubry, Bloch, and Meyer, 1921; Gallavardin, 1922; Warburg, 1928). Four additional cases are summarized below.

(1) *Kampmann (1935).*—A chauffeur, aged 43, was cranking his car when it back-fired and caused him to fall down. He felt a stinging sensation in his chest and shortly afterwards collapsed with severe chest pain. Vomiting and attacks of un-consciousness followed and he was admitted to hospital, where the heart rate was found to be 32–36. He recovered, but several Adams-Stokes attacks occurred later, the last one 22 months after the accident. A cardiogram taken over two years after the accident showed slight prolongation of the P–R interval.

(2) *Kissane (1937).*—A man, aged 35, passed as healthy at examination for life insurance nine months previously, was struck in the back by a slab of slating and doubled up. He felt a violent pain in his chest and was breathless. One month later the pulse was observed to be irregular, and he began to suffer from fainting fits. Six months after the accident examination showed enlargement of the heart and a systolic murmur. A cardiogram showed partial A-V block. He died nine months after the accident in a syncopal attack.

(3) *Coffen (1930).*—A healthy boy, aged 3, fell four feet, hitting his chest; no external injuries were noted. Next morning the heart rate was 65 and later in the day 50. The rate fell to 36 in the following few days. At the age of 10, complete heart block was recorded by cardiogram. There was a pulmonary systolic murmur and X-ray showed a prominence due to the left auricle.

(4) *Schilder (1935).*—A man, aged 66, giving a history of being kicked on the chest in childhood, had been subject to paroxysmal tachycardia for five years. Examination showed signs suggesting arteriosclerotic aortic stenosis and incompetence, hyper-tension, and cardiac enlargement. Aged 66, he was struck by a waggon shaft on the lower part of the sternum, following which he collapsed and remained unconscious for three-quarters of an hour. Bradycardia, rate 35, was noted within 15 minutes of the accident, and two days later 2 : 1 block was recorded. Frequent Adams-Stokes fits followed, in one of which he died, four months after the accident. Autopsy showed considerable hypertrophy of the heart and myocardial fibrosis. The coronary arteries were stenosed and calcified, but the valves were normal.

The prognosis in traumatic heart block is not always bad. Of the ten cases cited, four died while under observation; one lived 6 weeks, one 4 months, one 9 months, and one 13 years. The remaining cases were alive and under observation for periods of 1, 1 1/2, 4 1/2, and 5 years respectively: one, only observed for 3 months, was quite well. Heart block of undetermined ætiology is by no means rarely seen, especially in young subjects, and in some of these cases it may be due to trauma. In three of the cited cases with permanent

heart block due to trauma, the age at the time of injury was 3, 16, and 21 years respectively.

Sino-auricular Block.—Kissane (1937) has described a case of contusion of the heart in a soldier who was struck on the chest by a bayonet, near the apex beat. He became breathless and felt pain in the left chest and shoulder; a systolic murmur appeared at the apex. Eighteen years later a cardiogram showed sino-auricular block.

CHANGES IN THE VENTRICULAR COMPLEX OF THE CARDIOGRAM

The best evidence that injury has caused a myocardial lesion is a changed ventricular complex appearing immediately after the trauma. Usually the changes observed have been regressive, but occasionally progressive changes have been recorded.

My previous paper included 12 cases of injury that caused cardiographic changes such as heart block, auricular fibrillation, and flutter, and also QRS and T changes. My new material includes 8 further cases as follows : Kissane (1937), curves of posterior infarction; Kienle (1938), T wave changes of posterior infarction and nodal rhythm; Störmer (1938), T wave changes of posterior infarction; Smith and McKeown (1939), R–T elevation followed by T inversion associated with pericarditis; Kissane (1937), R–T elevation in lead III followed by low voltage curves; Meixner (1931), T inversion and slurring of QRS, followed by auricular fibrillation; Campbell (1939), low voltage T_2 and inversion of T_3; lastly my own case, summarized below.
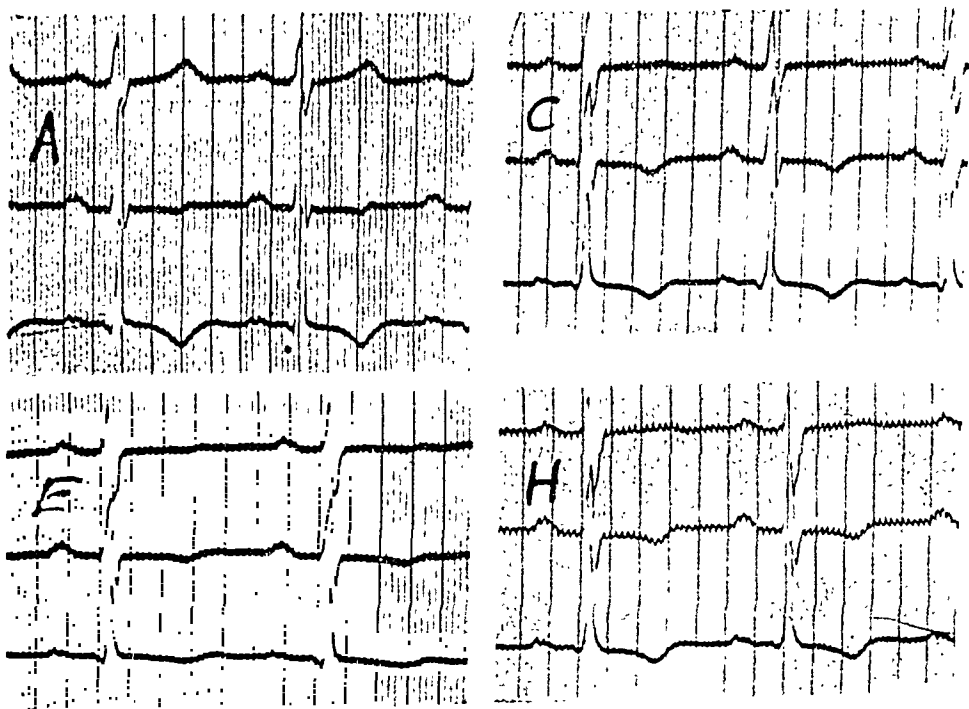
FIG. 1.—Serial cardiograms from case of myocardial trauma five months after the accident (A) April 13 ; (C) April 30 ; (E) May 16 ; (H) June 9, 1938 (leads I, II, and III from above downwards in each cardiogram).

Warburg (1938) (case communicated by Dr. Voght-Moller).—The patient had enjoyed good health up to November 1937, when he slipped and fell while loading turnips into a cart ; he felt pain in the chest radiating to the right arm, became breathless, sweated, and lay on the ground for five minutes. He was unable to work for some days, and after a temporary improvement became more breathless. Five months after the accident he was admitted to hospital suffering from violent attacks of pain in the chest combined with tachycardia, rate 160. Systolic and diastolic aortic murmurs were audible, with the Wassermann reaction negative. He died of cardiac failure eight months after the accident. During his stay in hospital, seven cardiograms were obtained, four shown in Fig. 1. The later curves show inversion of T in leads II and III and an isoelectric T in lead I.

Autopsy.—Heart weight, 270 g. No pericarditis. Right auricle distended ; left auricle normal. Valves normal. Ventricles normal. Just below the aortic valves a minute yellowish thickening of the endocardium of the left ventricle. Coronary arteries normal. Section of the heart showed a thin area on the lower posterior wall of the right auricle to which a few small thrombi were adherent, and the auricular appendix also contained thrombi. Sections of the ventricular and septal muscle showed no appreciable abnormality.

Thus at least 23 cases with transitory changes in the cardiogram following injury have been reported; 2 of these are known to have died after nine months and five years respectively. In 14 cases the period of observation varied from a few weeks up to seven years. In 8 cases recovery was stated to be complete. Thus the prognosis in the milder cases is good, especially if the patient is not too old and has not had previous cardiac symptoms.

Auricular Fibrillation

Auricular fibrillation is not rare in traumatic myocardial lesions, and my previous review included 41 cases of established and 4 of transitory fibrillation or flutter. The new material includes 10 cases of complete irregularity, i.e. one fifth of all cases, as in my previous series.

The new cases are summarized below.

(1) *Jervell (1933).*—An athlete, healthy when examined previously, was knocked down by a car, which struck the back of his chest. Shortly afterwards the pulse became rapid and irregular ; a cardiogram, nine months later, showed auricular fibrillation. Normal rhythm was restored by quinidine and the patient remained well during two years' observation.

(2) *Bramwell (1934).*—A mason, aged 35, previously healthy, struck his head against a beam ; he vomited and had severe headache for some days. Nine days after the accident auricular fibrillation was found, without cardiac enlargement or signs of failure. Neurological examination was negative. Normal rhythm was restored by quinidine and he was well a year later.

(3) *Barber (1938).*—A healthy man, aged 58, was hit on the head by a signboard and entered hospital with an injury of the cervical spine. His pulse, at first 80-90, accelerated to 120 after ten days, and a cardiogram three months later showed auricular flutter. Heart enlarged : B.P. 160/100 mm.

(4) *Barber (1938).*—A man, aged 61, was admitted to hospital after being run down by a car, and a few days later his pulse became irregular. His capacity for work diminished, and eleven months later a cardiogram showed fibrillation, apart from which the heart was normal. Five years later there was no change.

(5) *Barber (1938).*—A man, aged 63, was run down by a car, and on admission to

hospital a cardiac irregularity was noted. On leaving hospital he was breathless, and six weeks after the accident a cardiogram showed auricular fibrillation ; otherwise the heart was normal.

(6) *Kissane (1937)*.—A man, aged 45, previously healthy, was hit on the back by a slab of slate and fell against a waggon, fracturing the second and third left ribs. Dyspnœa, pain in the chest, and hæmoptysis followed, and auricular fibrillation developed. Two years later there was cardiac enlargement and failure. A cardiogram showed fibrillation. Six years after the accident he was worse.

(7) *Kissane (1937)*.—A man, aged 55, previously healthy, was struck on the sternum in a motor accident, and on admission to hospital the heart was irregular. He suffered from dyspnœa and sternal pain on effort, and, six months later, had a cerebral embolism. Nine months after the accident there was auricular fibrillation, cardiac enlargement, and signs of failure.

(8) *Moritz and Atkins (1938)*.—A man, aged 74, was run down by a car, sustaining extensive injuries including fractures of two ribs. Auricular fibrillation developed the next day, and he died of heart failure ten days afterwards. Necropsy showed fibrinous pericarditis, hæmorrhages into the right auricle, extensive coronary sclerosis without recent thrombosis, and hæmorrhagic necrosis in an old infarcation of the right ventricle, regarded as of traumatic origin.

(9) *O'Farrell (1939)*.—A man, aged 59, experienced severe pain in the left chest and dyspnœa, after a motor accident. There was fracture of a left lower rib. Three weeks later he had an attack of dyspnœa and auricular fibrillation was found. He died of heart failure three months after the accident. Necropsy showed a left pleural effusion, pericardial thickening, and adhesions at the apex, covering a cardiac aneurysm and myocardial fibrosis. Slight sclerosis of mitral and aortic valves. No coronary occlusion.

Thus of 10 cases of fibrillation, 2 recovered completely, 2 died ten days and three months after the accident respectively, and the remaining 6 showed signs of cardiac impairment.

EXTRASYSTOLES

Extrasystoles following trauma have seldom been reported. My original paper included 9 cases and there are only 2 additional ones. Barber's patient, a syphilitic, was injured by a bull, fracturing three ribs, after which the pulse was irregular from frequent extrasystoles, and remained so a year later. Meixner's patient, besides extrasystoles, had T wave abnormalities in the cardiogram.

ANGINA PECTORIS

The possibility of angina pectoris being caused by trauma was first discussed by Hans Kohn (1929), who collected 4 cases; 2 of these seem doubtful and 2 had syphilitic aortitis, making it difficult to decide the role of trauma in the pathogenesis of the anginal syndrome. I was able to collect 13 published cases and to add 6 cases of my own, but only two thirds of these 19 cases could be accepted as well-substantiated.

Excluding cases in which the history was inadequate or in which the interpretation of the anginal symptoms was doubtful, my new material includes 16 cases of angina pectoris following trauma, as follows: Kampmann (1935),

Kissane (1937) 4 cases, Kienle (1938), Störmer (1938), Barber (1938) 4 cases, Peters (1938) 2 cases, Wüllenweber (1939), Dahle (1939), and Warburg (1938).

These cases were mostly men over 40 years of age, who had been in good health prior to accidents that often involved injury to the chest, and developed anginal pain shortly afterwards. The following two cases may be cited as examples.

(1) *Peters (1938)*.—A man, aged 54, free from cardiac symptoms, was involved in a car accident, fracturing his right arm. He was in severe pain for two days, and a week later developed oppression in the left chest and arm. There were no abnormal signs in the heart and the blood pressure was normal. He died during a severe anginal attack a fortnight after the accident. Necropsy: coronary sclerosis without occlusion; mild fibrosis and fatty infiltration of the myocardium. An insurance company refused to accept the accident as the cause of death.

(2) *Warburg (1938)*.—A man, aged 62, previously healthy except for glycosuria, had a cycle accident in 1935 which caused a swelling in one rib. In April 1937 he was run over by a car. He continued his work with difficulty for a week, after which he developed severe pain in the chest and stayed in bed for two days. On attempting to return to work he again had violent mid-sternal pain extending to both arms, and had to return to bed. After this he was unable to work until January 1938. In August 1938 he was subject to typical angina of effort, but was able to do light work. Examination showed the pulse regular, rate 48. Blood pressure, 180/80 mm. No signs of heart failure. X-ray and cardiogram showed no abnormality.

In most cases the pathogenesis of the anginal pain is probably explained by a vascular lesion ; but Peters suggested that peripheral stimulation from a broken arm caused coronary spasm, and Wüllenweber suggested interference with the coronary vasodilator fibres in a case with injury to the spinal cord.

My previous study included 2 cases of coronary thrombosis and 1 case of injury to a coronary branch following accidents, and I know of 6 other cases of traumatic coronary occlusion. The following may be cited as examples.

Fraenkel (1917).—A soldier, aged 20, was wounded by a shell explosion which caused an injury to his right arm and also concussion. He died six months later with cardiac failure. Necropsy showed an aneurysm of the left ventricle due to an aneurysmal dilatation of the left descending coronary artery, which was blocked by thrombi. The lesion was attributed to general concussion due to the shell injury.

Muller (personal communication).—A barrister, aged 59, free from cardiac symptoms, was run over by a bicycle, falling on to his thorax and abdomen. He sustained no external injuries and was able to get up immediately and walk to his office. He continued his work during the following days, though he did not feel well and experienced substernal oppression when walking upstairs or uphill. Nine days after the accident he had a severe nocturnal anginal attack and was admitted to hospital. The clinical picture became typical of cardiac infarction ; there was fever, leucocytosis, and typical R–T changes in the cardiogram. He died two weeks after the accident, with cardiac failure. Necropsy showed thrombotic occlusion of the left descending coronary artery with a large cardiac infarct and recent pericarditis. There was arteriosclerosis of the occluded branch and to a lesser degree of other branches.

Non-penetrating Cardiac Injuries in Children

Hawkes (1935) reported the following case of cardiac aneurysm. A boy, six years old, was hit by a truck. The diagnosis was compression of the chest and multiple abrasions of the body. He was discharged after one week as cured. He continued his usual life at home until three months after the accident, when he came home from school feeling sick. While eating his supper he fell off his chair, dead. At autopsy a ruptured traumatic aneurysm of the left ventricle with hæmopericardium was found. The aneurysm was globular, thin-walled, and on the posterior surface of the ventricle. It measured 4 cm. in diameter with a rupture at the summit, 0·5 cm. in diameter. No rheumatic or syphilitic lesion was found. There was no chest wall injury or fracture.

Gunewardene (1924) has described the case of a boy, aged 9, who was crushed against a wall without receiving any obvious injuries. Ten days later he died suddenly while playing at school. Necropsy showed hæmopericardium from rupture of the left ventricle. Similar cases described by Groom (1897) and by O'Neill (1914) were cited in my original paper.

Site and Type of Injury

In almost all cases in which the site of the injury has been stated, the thorax has been involved, usually by being struck from the front. In several cases the back was hurt, in one the right shoulder, in one the head, and two patients fell on their buttocks. Injuries distant from the heart may damage it, though very rarely. The accidents occurring in the present series of cases were similar in nature to those in the first series, and are tabulated below. Details were given in 57 of the 59 cases.

Fall	18 cases
Blow from plank, etc.	10 „
Run into or run over	9 „
Ran into something	6 „
Injured by steering-wheel	4 „
Hit by a waggon shaft	3 „
Fist blow	2 „
Injured by starting-handle of car	1 case
Jammed	1 „
Pushed by bull	1 „
Bayonet lesion	1 „
Shell injury	1 „

Diagnosis

The diagnosis of traumatic myocardial disease depends on a careful history. Often the heart is not perfectly normal prior to the accident, and both arteriosclerosis and hypertension may be predisposing factors. This was so in 10 cases of my first series and in 14 cases of the new series. Meixner (1931) in discussing this question concluded that the coronary arteries were frequently affected in sudden exertion or in sudden falls, and that if there should happen to be a lesion making them susceptible to rupture, a coronary thrombosis might occur owing to rupture of the intima; or, on the other hand, an aneurysm of the

ventricle might occur with subsequent rupture, or a pericarditis with subsequent rupture of the auricle. Difficulty may arise because, in some cases, the patient's condition immediately following the accident is not conspicuously bad. More often than not the patients do not faint, and in the present 59 cases fainting was specified in only 4, while in 24 absence of fainting was explicitly stated. There may be a latent period of a few days up to several months between the accident and the appearance of cardiac symptoms, as happened in 10 of the present cases. Almost every known abnormality of the electro-cardiogram has been observed, yet in many cases there was no abnormality.

PROGNOSIS

It is impossible to generalize about prognosis. The present material includes cases that recovered within a few weeks, many that developed chronic heart failure, and others that died fairly soon after the injury. Of my previous series, 74 patients are known to have died from their traumatic cardiac lesion and in the present series 16 out of 59 cases ended fatally. The period of survival is known in 14 of these cases and was 7 days, 10 days, 10 days, 2 weeks, 3 months, 3 months, 4 months, 9 months, and 2 years respectively.

SUMMARY

Another 59 cases of myocardial or pericardial damage due to non-penetrating blunt injuries have been collected and are reviewed with data from a previous series of 202 similar cases.

The traumatic cardiac lesions described include pericarditis, heart block, myocardial damage, auricular fibrillation and other disturbances of rhythm, and angina pectoris. Auricular fibrillation occurred in a fifth and angina pectoris in a quarter of these 59 cases. Seven cases of traumatic coronary thrombosis are cited.

In almost all cases the injury involved the thorax, sometimes fracturing one or more ribs, but in a small proportion injuries distant from the heart were responsible for cardiac damage.

Arteriosclerosis and hypertension were sometimes present and may have rendered the heart more susceptible to injury from violence to the chest.

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THE VASCULAR RESPONSE IN CHRONIC RHEUMATOID ARTHRITIS

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It has been suggested that a deficient blood supply might bring about abnormalities in the joints, just as it can in other tissues, and that vascular disturbances might be an ætiological factor in the causation of rheumatoid arthritis and osteo-arthritis. Savage and Taylor (1939) by means of oxygen and carbon dioxide measurements in the joints have shown that in certain cases of these diseases such a deficiency may exist. Goldhaft, Wright, and Pemberton (1933) successfully repeated the work of Wollenberg (1909) who showed that ligation of the patellar blood vessels in a dog produced symptoms of hypertrophic arthritis. The relationship between lack of blood supply and osteo-arthritis is illustrated by the following case seen by one of us. A man of 59 years of age suffered for five years from pains in the left knee and hip, the area round the latter being dead cold to the touch. The X-ray examination showed marked osteo-arthritis in the left hip, the presence of some unabsorbed material on this side, and distinct signs of arteriosclerosis in the left lower thigh. The patient stated that the only injections he had received were of gold into both buttocks two years ago. The non-absorption of this material, together with arteriosclerosis and coldness, on the affected side only, pointed to a deficient blood supply.

Many rheumatic subjects are very sensitive to cold weather and complain of cold hands and feet, and this has led to many investigations on skin capillaries. Deviations from the normal have been described, such as constriction (Lunedei and Coradini, 1930, and Bisset and Woodmansey, 1932); decrease in the number of capillaries above joints, where there were Heberden's nodes, and where the capillaries were also constricted (Kovacs, Wright, and Duryee, 1933): these authors saw tortuosity of the small skin vessels in 60 per cent of cases of osteo-arthritis in comparison with 35 per cent in respect of rheumatoid arthritis, but they attribute this to the higher age of the former; they conclude that many changes from normal do occur in the skin capillaries and skin temperature, but owing to the lack of consistency of the observations they can not be considered as responsible for the pathological changes. Kersley (1937) agrees with this view.

The problem therefore is whether, apart from obstructed blood flow to the

joints, there is any functional vascular abnormality that leads to changes in the joints in cases of rheumatoid arthritis of unknown origin. Disturbance in the vascular constrictor tone is likely to be suspected, as it is met with in the so-called Raynaud syndrome and in acrocyanosis. In both these maladies the arteriolar constrictor tone is increased and in acrocyanosis there is also atonia of the subpapillary venous plexuses of the skin. Patients suffering from these vascular disorders are, like rheumatic subjects, very susceptible to cold. If in rheumatic diseases abnormal tone is present, one would expect a reaction to heat and cold similar to that in Raynaud's syndrome or in acrocyanosis. A suitable means to test such a vascular response is by the use of contrast baths.

The normal reaction of the blood vessels to this type of bath has been determined by Uprus, Gaylor, and Carmichael (1936). Our experiments are based on the fact observed by Gibbon and Landis (1932) that immersing one forearm in hot water produced vasodilatation in the other arm as well. More particularly Woodmansey, Collins, and Ernst (1938) have studied this reaction in rheumatic subjects. The times of immersion which these authors employed were too short for any sufficient vascular response.

METHOD

The usual method of finding if the capillaries are dilated or constricted is by measurements of the skin temperature. We used the nail bed of the index or third finger. According to Lewis and Pickering (1933) this shows the earliest response when the arm is exposed to hot or cold air, owing to the presence of numerous arterio-venous anastomoses at the finger tips (Grant and Bland, 1931). Gibbon and Landis (1932) have confirmed such response when the arm is heated with warm water.

Skin temperature measurements were carried out by us using the well known thermocouple-galvanometer method. The room was kept at as constant a temperature as possible during an experiment, but it varied somewhat from day to day from 18° to 21° C. The subject was seated comfortably in a chair so that the arms were able to relax. The two thermocouples were fixed one on each hand, usually at the nail bed of the index, but sometimes of the third finger. Measurements were carried out at intervals, until the temperature of the digits showed a constant figure, usually after 10–20 minutes, but exceptionally after 40 minutes. One arm was then immersed in a large bowl containing warm or cold water, as the case might be. The temperature of the warm water was kept constant by an immersion heater. The temperature of the cold water changed very little in the short time (8–12 minutes) during which the arm was immersed. The amount of water was sufficient to cover the arm from the middle of the hand up to the middle of the biceps. The finger to which the thermocouple was attached remained well above the surface of the water. Temperature readings were noted at intervals of half a minute to two minutes, from the digits of the immersed and non-immersed arms. When satisfactory readings had been taken of the response to heat or cold, as the case might be, the hot water was changed for cold or vice versa. This process was repeated several times. It was not found possible to measure the rectal temper-

ature during an experiment, and we had to be satisfied with mouth temperatures. This invariably rose by 0·4°–0·5° C. when the arm was immersed in hot water, and fell (0·2°–0·3° C.) when the arm was immersed in cold water, a point which has already been discussed by other writers.

OBSERVATIONS ON THE REACTION TO CONTRAST BATHS

These have been carried out on the following groups:—

(A) Normal subjects (10 cases)

(B) Non-arthritic subjects with Raynaud's syndrome in various stages (such as when cold- or warm-handed) (8 cases)

(C) Non-arthritic subjects with acrocyanosis (5 cases)

(D) Subjects with rheumatoid arthritis—

       (*a*) with a normal blood sedimentation rate (21 cases) ;

       (*b*) with a raised blood sedimentation rate (9 cases).

We have selected from each group cases that showed a typical reaction.

(A) *Normal subjects*

The main features of the response of a normal subject to contrast baths are shown in Fig. 1.

(*a*) In cold water there is an immediate rapid fall in the temperature of the fingers of both the immersed and non-immersed arms.

(*b*) In hot water this fall continues for a short period (5–8 minutes) and is followed by a rapid rise of both fingers.
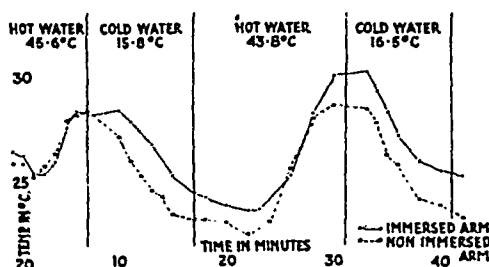
FIG. 1.—Normal subject, aged 38. In hot water there is a short fall in temperature, followed by a rapid rise in the digits of both the immersed and non-immersed arms. In cold water a rapid fall in temperature of both sides is shown. On immersion again in hot water there is a rapid rise in temperature after a delay of 6 minutes. After this cold water produces the usual rapid fall.

We found that if the initial skin temperature was high, that is if the arm was already in a state of vascular dilatation, then immersion in hot water could only produce a slight increase in this state.

(B) *Non-Arthritic subjects with Raynaud's Syndrome*

In general, patients suffering from this vascular disorder showed when they were warm-handed a normal or nearly normal response. When they were cold-handed the response was greatly delayed; but, once established, was normal in character. Variations occurred both from subject to subject and in the same subject at different times.

Observations on a typical case were as follows:

A woman, aged 33, had suffered for several years from cold arms, hands, and feet. Two years before sympathectomy had been performed on one leg without any effect on the Raynaud's syndrome. In particular the left hand and arm felt very cold, and the little finger showed marked cyanosis. Sometimes, however, the temperature of the hands was quite normal. There were no symptoms of arthritis or of heart failure.

We found variable reactions such as the following :

1. A complete lack of response to both heat and cold in both hands. The initial temperature of the digits was low (20·8° C. on the immersed, 20·3° C. on the non-immersed side). Cold water at 14° C. caused a drop in temperature on the immersed side to 17·9° C. in 10 minutes. On immersion in hot water at 45·5° C. no rise occurred even after 20 minutes' immersion. Subsequent immersion in hot or cold water could not release the vaso-constriction (see Fig. 2).
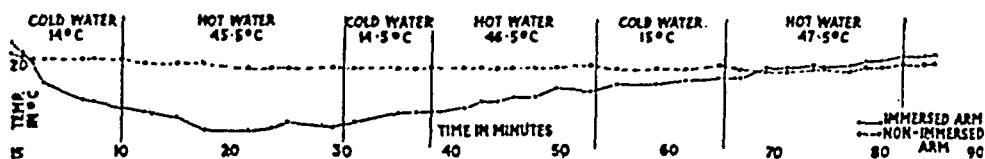
FIG. 2.—Subject suffering from Raynaud's syndrome. When cold-handed, practically no response in either side occurs, though at first the immersed hand becomes a little colder.

2. No response for a long time on the immersed side (initial temperature 20·4° C.) either in hot or cold, whilst the non-immersed arm (initial temperature 23·4° C.) had the paradoxical response of a rise in cold water at the beginning (see Fig. 3).
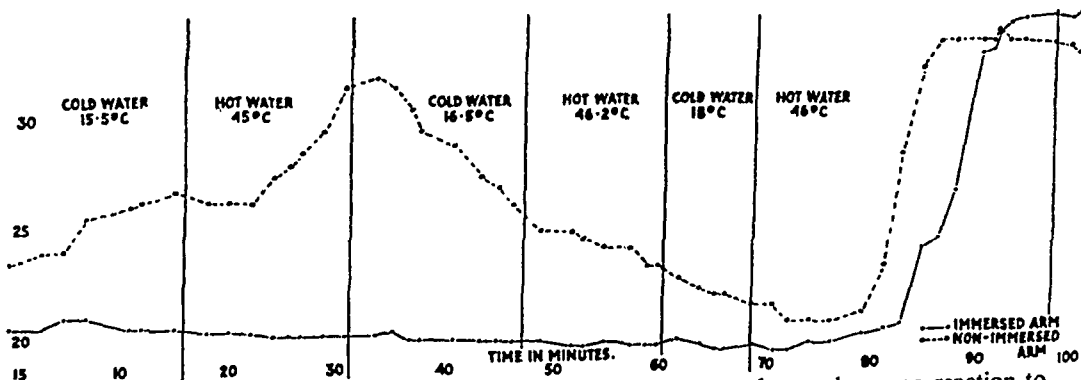
FIG. 3.—Subject suffering from Raynaud's syndrome. Immersed arm shows no reaction to heat or cold for a long time. A paradoxical rise in the temperature of the non-immersed arm to the stimulus of cold is shown; as also is the rapid response on both sides when this rise has gradually passed off.

3. When the same subject was investigated at a time that he was free from symptoms and warm-handed, an almost normal response was obtained on the immersed side, while the non-immersed side, after reacting poorly to cold, showed a normal response.

(C) *Non-Arthritic subjects with Acrocyanosis*

In general, subjects suffering from this disorder can show an almost normal reaction even when cold-handed; it is, however, characterized by the suddenness of the response to heat. On the other hand, after immersion in cold water, the vaso-constriction may become so intense that a response similar to Raynaud's syndrome when cold-handed is obtained. When response was established either to heat or cold, the graph representing the reaction did not proceed smoothly but showed an unexplained jerkiness.

The following case may be taken as typical: A woman, aged 27, had suffered from acrocyanosis in the hands, feet, and lower part of the legs for many years. There were no signs of disturbance in the endocrine glands nor of heart failure. Both hands felt cold to the touch and had a bluish-red colour. There were no signs of arthritis.

1. Sometimes there was a reaction that resembled the normal.
2. In another observation hot water produced a rise in temperature of both digits similar to a normal reaction, but more rapid. When immersed in cold water again there was a rapid fall in temperature which continued, when the arm was again immersed in hot water, for a long period, and no rise in temperature occurred (see Fig. 4).
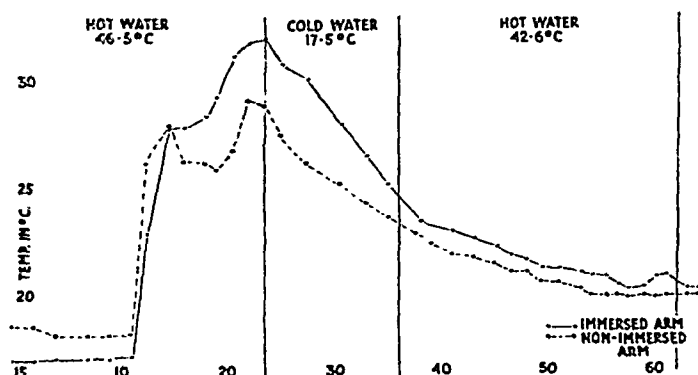
FIG. 4.—Subject suffering from acrocyanosis. The sudden rise in temperature of both sides follows the usual initial delay in hot water. Cold water produces an immediate fall in temperature, which continues on subsequent immersion in hot water, the latter failing to release the vaso-constriction even after 26 minutes' immersion.

(D) *Subjects suffering from Rheumatoid Arthritis*

(a) *With a normal blood sedimentation rate* (21 *cases*)

These subjects gave a typically normal response. Many observations were carried out at various times on each of these subjects in addition to many others, and all of them showed a normal reaction.

The following may be given as an example: A woman, aged 48, had hysterectomy performed 15 years ago, having previously had three normal births. B.P. was 170/110 mm. She had suffered from painful swelling in the right knee for three years. No marked bony changes were shown on X-ray examination. Blood sedimentation rate 5 (Westergreen method, 1 hour). The illustration has not been reproduced as it was similar to Figs. 1 and 5.

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(b) *With a raised blood sedimentation rate* (9 cases)

The results obtained may be given under the following headings:

1. Rheumatoid arthritis, without any abnormalities of posture, showed a normal response to heat and cold.

2. Rheumatoid arthritis, characterized by a long history of infectious diseases and with marked anatomical changes in the joints associated with postural defects, gave a sluggish response at each observation.

The following cases may be given as examples :—

A woman, aged 58, had suffered from rheumatism after her first pregnancy. For some years she had pains in her finger joints and wrists with severe recurrent swelling and pain.   On X-ray examination destructive changes in some meta-carpo-phalangeal joints.   The blood sedimentation rate was between 14 and 19.
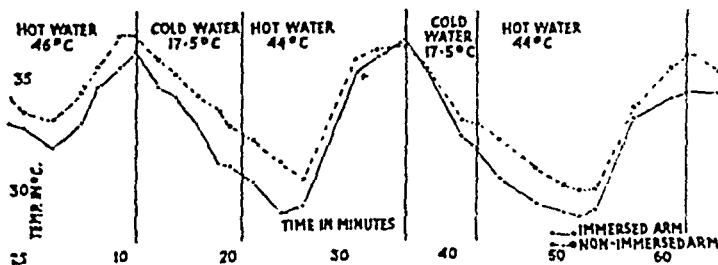
FIG. 5.—Subject with rheumatoid arthritis (raised blood sedimentation rate).   A typically normal response.

A woman, aged 28, had suffered from many infections in childhood, but not from rheumatic fever.   After scarlet fever rheumatic pains started with swelling in the hands, ankles, and elbows, and with iridocyclitis of the left eye· Her general condition was poor and she could not walk without orthopædic support because of severe deformities in both hands and feet.   X-ray examin-ation of the hands showed chronic rheumatoid arthritis with bony fusion of the carpal bones and ankylosis of several phalangeal joints.   She had very pronounced deformities of the hands and arms.   Her blood sedimentation rate was 40.   There was a sluggish rise in temperature on the immersed side, while the non-immersed side showed a normal response (Fig. 6).
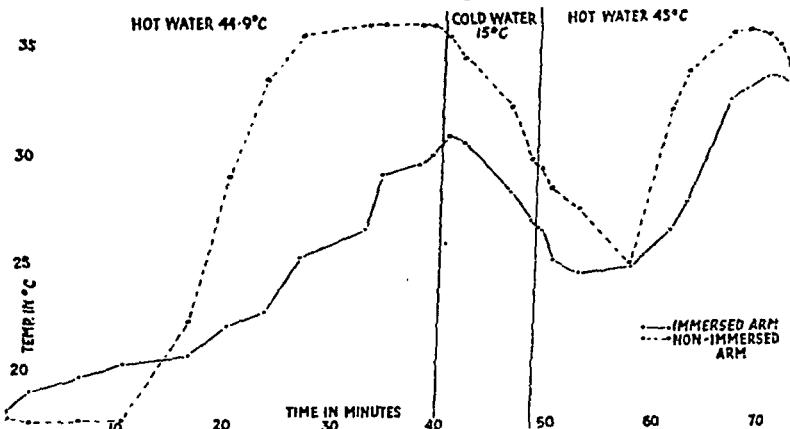
FIG. 6.—Subject with rheumatoid arthritis and postural deformities (raised blood sedimentation rate).   A sluggish rise in temperature on the immersed side occurs while the non-immersed shows a normal response.

Discussion

The general features of the response of normal subjects to heat and cold closely resemble those obtained by Lewis and Pickering (1931–33), by Uprus, Gaylor, and Carmichael (1936), and by Gibbon and Landis (1932), although the actual limbs used and the procedure differed somewhat. Cooling one arm produces an immediate fall in temperature; heating one arm produces a delayed rise in temperature of both the immersed and non-immersed arm lasting from 8 to 10 minutes. Carmichael *et al.* (1936) pointed out that two factors are responsible for the cooling effect; the sensory stimulus producing vaso-constriction, and the cooling of the blood. The stimulus for the vascular dilatation is the rise in blood temperature; this must overcome the vaso-constrictor tone which may vary from subject to subject. When a normal subject was investigated, at one time with warm, and at another time with cold hands, the heat response under the latter conditions showed a delay which did not, however, exceed 8–10 minutes. Lewis and Pickering (1931–33) have shown that dilatation begins in the warmer fingers; the delay in response of the cooler fingers is attributed to the direct constrictor effect of cold on the arterioles. In cases of so-called Raynaud's syndrome with cold hands, when an increased vaso-constrictor tone is known to be present, not only is the time required to release the vaso-constriction lengthened, but the characteristics of such a response in the immersed and non-immersed limbs may be entirely different. In this vascular disorder we noted three principal types of reactions:

(*a*) the vaso-constrictor tone may remain unchanged in both arms;

(*b*) the vaso-constrictor tone may be released in one arm only, whilst the other side remains constricted;

(*c*) a paradoxical rise in cold and a fall in hot water may occur.

Once the reaction is initiated on both sides, it continues to be normal in type, as Lewis and Pickering have already pointed out. In acrocyanosis a rapid heat response may be obtained. However, after immersion of one limb in cold water the vaso-constrictor effect produced may be so great that subsequent immersion in hot water fails to release it.

In our subjects with rheumatoid arthritis of various types we have found no similarity, in their reaction to contrast baths, to these fundamental types of functional vascular disturbance. Rheumatoid arthritis and Raynaud's disease are only occasionally associated, whereas one would expect this more frequently if functional vascular disturbance were an ætiological factor in arthritis. One case of Raynaud's syndrome in which arthritic changes in the terminal joints of the finger were observed has been described by Lewis (1937); the changes were considered to be due to old re-canalized thrombi which severely restricted the blood flow to these joints—an anatomical cause for the condition.

The reaction of our arthritic subjects was tested on many different occasions in order to detect a possible temporary disturbance of vascular function; but even when the temperature of the hands was low, a quite normal response was obtained. Nor was there any sign of vaso-constriction that could not be released, such as occurs in acrocyanosis. The delay in heat response in these cases after immersion in cold water did not exceed the time observed in normal

subjects. A distinct delay in heat reaction was, however, noted in a severe case of rheumatoid arthritis of long standing, high sedimentation rate, and marked deformities of the arms and hands. Other subjects with all the same changes except the postural abnormalities gave a normal reaction. It has been found out by Uprus, Gaylor, Williams, and Carmichael (1935) that limbs with an abnormality in posture show a pronounced delay in heat response, which could also be elicited from a normal subject who imitated this abnormal posture. We are justified, therefore, in attributing the result in rheumatoid arthritis to this cause.

We conclude, that as far as the vascular system is concerned in the ætiology of rheumatoid arthritis and osteo-arthritis, a permanent arrest of blood flow caused by thrombi, by severe arteriosclerosis, or by any mechanical means, may produce joint and bony changes. In cases of vascular disorders like Raynaud's syndrome when associated with arthritis one has to consider the possibility of obstruction of the vessels leading to the affected area. No specific nor particular type of functional vascular reaction, as tested in contrast baths, could, however, be elicited in the various forms or stages of rheumatoid arthritis that we were able to investigate. This does not exclude the fact that many rheumatic patients are especially sensitive to cold, but this cannot be ascribed to abnormal vascular constrictor tone.

SUMMARY

1. Arthritic changes have been seen in cases in which the blood supply to a joint has been restricted.

2. Investigations have been carried out to find if there might be any functional vascular disturbance in various types and stages of chronic rheumatoid arthritis. The reaction of rheumatic subjects to contrast baths has been compared with that of normal subjects and of subjects suffering from increased vaso-constrictor tone such as Raynaud's syndrome or acrocyanosis.

3. Unless a marked postural deformity was present all rheumatic subjects showed a reaction well within normal limits.

4. Several types of reaction to contrast baths were obtained in cases of so-called Raynaud's syndrome and acrocyanosis. There was no similarity to the reactions obtained in cases of rheumatoid arthritis.

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THE HEART RATE DURING A SIMPLE EXERCISE

BY

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Simple exercise tolerance tests, such as stepping on and off a stool a given number of times and noting the effect on the pulse rate, have long been used in medical practice. Almost invariably, however, the pulse rate is taken before and after, owing to the difficulty of counting it during the exercise. This may be overcome by means of a recording apparatus such as that of Bell and Knox (1938); the R–S waves of the electrocardiogram are recorded on a smoked drum, and the amplifier is modified to minimize the effects of skeletal muscle activity. Time in seconds, respiration, and signals for the beginning and end of exercise are also recorded on the drum, and thus a very complete and accurate analysis of the heart rate during even a short exercise is possible. Fig. 1 shows a normal trace obtained by this method.
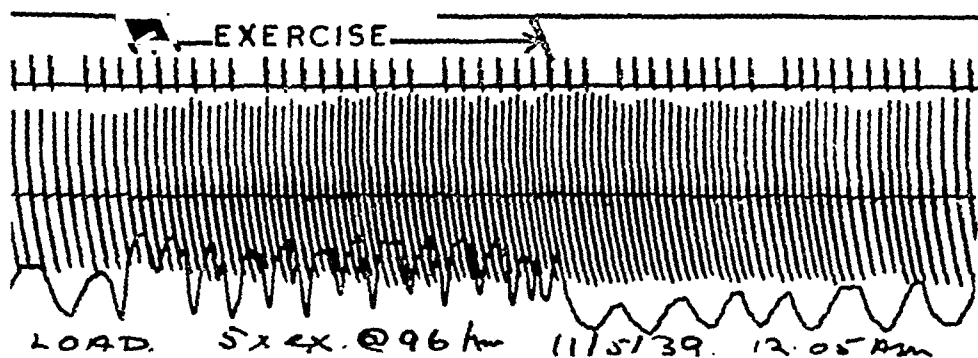
FIG. 1.—Portion of normal tracing showing the response to exercise. Upper tracing, signal showing the start and stop of the exercise. Second tracing, time in seconds, with a break once in 10 seconds. Third tracing, heart beats. Fourth tracing, respiration (the rise of the lever indicates expiration).

The exercise adopted as standard for this series is light enough to be suitable for many cardiac patients, and the movements required, viz. those of stair-climbing, enter into the routine of daily life. The advantage of this was pointed out by Master and Oppenheimer (1929) and by White (1937).

Seventy-five male medical students acted as subjects. They were in good health, but were not in training. Their ages, in nearly every case, lay between 18 and 22 years.

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The Tolerance Test

As the test is designed with a view to clinical use, no extreme precautions are taken for obtaining a true basal initial rate, and slight latitude is allowed in the performance of the exercise. The subject first has a brief practice in ascending the steps, and after the chest electrodes and stethograph have been applied, he sits down on a chair eighteen inches high and relaxes as fully as possible.

The two chest electrodes employed are saucer-shaped copper discs 2·5 cm. in diameter. The concavity is filled with soft green soap which acts as the electrolyte, as recommended by Bell, Knox, and Small (1939). The electrodes are kept in contact with the chest by means of light elastic straps. One electrode is applied over the apex beat and the other over the second right costal cartilage. A satisfactory voltage and an even base line are obtained with the electrodes in these positions.

At the end of three minutes a tracing is run for 30 seconds, the subject remaining relaxed. The drum is then stopped and a further two minutes' rest allowed, giving five minutes in all; Master (1934) stated that this is usually sufficient to reach a steady resting rate. The drum is then started and the resting heart rate recorded for 15–20 seconds, after which the signal to start the exercise is given. The subject rises to his feet, steps five times up and down two steps each ten inches high and then sits down again and relaxes. To standardize the rate of climb the subject steps in time with a metronome beating 96 per minute. The average duration of the exercise from rising to sitting again is 24 seconds. It will thus be seen that the standard exercise of the present test is both lighter and of much shorter duration than that of the usual type of cardiac tolerance test.

Method of Analysing the Tracings

Fine vertical lines are drawn across the tracings at intervals of 5 seconds, starting 10 seconds before the beginning of the exercise. The heart rate is then counted (to the nearest tenth of a beat) in each of these intervals of 5 seconds, and the highest rate obtained is converted to beats per minute; this is taken as the maximum rate. The time to reach the maximum rate is taken from the beginning of exercise to the middle of the 5-seconds period with the maximum rate. For example, if the maximum rate is found in the third 5 seconds from the beginning of the exercise the time to reach the maximum rate is 12·5 seconds.

The heart rate in the 10 seconds immediately preceding the beginning of the exercise, converted to beats per minute, is taken as the initial rate.

The actual increase in beats per minute of the maximum rate over the initial rate is given, and this is also expressed as a percentage of the initial rate (percentage increase on initial rate).

The acceleration of the heart rate in beats-per-minute per second is calculated by subtracting the rate in the 5 seconds immediately preceding exercise (converted to beats per minute) from the maximum rate, and dividing the result by the time taken to reach the maximum rate.

Another index which may prove of interest is the number of extra heart

beats induced by the exercise. This is calculated by subtracting half the initial rate (in beats per minute) from the number of beats in the 30 seconds after starting the exercise, this including the whole of the exercise period.

To get an index that does not require the use of apparatus, the heart rate is counted over the 30 seconds beginning 5 seconds after exercise ends, this being called the post-exercise rate and expressed in beats per minute.

Example of the Analysis of a Typical Tracing

The heart beats in the successive 5 seconds, starting 10 seconds before the beginning of exercise, were as follows: 6·9, 7·0, 8·2, 10·0, 10·7, 10·5, 9·1, 8·6, 8·4. The duration of exercise was 25 seconds. The initial rate is therefore $(6·9 + 7·0) \times 6 = 83·4$ beats per minute.

The maximum rate is $10·7 \times 12 = 128·4$ beats per minute, and it occurs in the third 5 seconds from the beginning of exercise; therefore the time to reach the maximum rate is taken as 12·5 seconds.

The acceleration of the heart rate is $(128·4 - 83·4) \div 12·5 = 3·60$ beats-per-minute per second.

The number of beats in the 30 seconds after exercise began was 57. Thus the number of extra beats induced by the exercise was $57 - 1/2(83·4) = 15·3$ beats.

The percentage increase on the initial rate was $(128·4 - 83·4) \times 100 \div 83·4 = 54$ per cent.

The actual increase in beats per minute was $128·4 - 83·4 = 45$ beats per minute.

The results are shown in Table I.

TABLE I

THE RISE OF PULSE RATE WITH THIS EXERCISE TOLERANCE TEST IN 75 HEALTHY MALE STUDENTS

Index	Mean	Range	Standard Deviation	Coefficient of Variation, Percentage
Initial rate, beats per minute..	85·7	59–121	13·8	16·1
Maximum rate, beats per minute	130·2	109–168	12·9	9·9
Time to reach maximum rate (seconds)	15·0	7·5–22·5	—	—
Acceleration per second of heart rate in beats per minute	3·0	1·4–5·3	0·9	28·7
Extra beats	17·0	8·6–27·2	4·9	28·6
Percentage increase on initial rate	53·9	19·8–100	18·5	34·3
Actual increase in beats per minute..	44·4	25–69	10·1	22·8
Rate after exercise, beats per minute	91·7	60–134	14·8	16·2

DISCUSSION OF RESULTS

(1) *Initial Rate.*—The mean rate of 85·7 beats per minute is somewhat higher than might be expected. The average sitting pulse rate in a corresponding age group was found to be 71–72 per minute by Volkmann (1850), and 70–72 per minute by McCurdy and Larson (1939), though Langowoy

(1900) gave an average of 80 per minute in a small series. The high initial rate of the present series is probably the result of psychological factors, as the subjects know that the exercise is about to start, though care is taken to see that the apparatus is not visible to them. This is borne out by the fact that the average heart rate taken after the first three minutes of rest is 81·5 per minute, while after a further two minutes of rest it has risen to 85·7 per minute just before exercise. Peabody and Sturgis (1922) found the same effect in normal subjects and in cardiac patients, and Addis (1922) showed the effect of excitement on the resting pulse rate. The accelerating action of mental factors on the heart was also pointed out by Gillespie (1924), Grollman (1929), and Ellis (1932).

Data on the variability of the sitting pulse rate appear to be very scanty, but Addis (1922) gave the average recumbent basal pulse rate as 80 per minute, and Jackson (1927) found an average recumbent rate of 80·2 per minute in 1600 male students, the coefficients of variation being 16 and 15·1 per cent respectively. Thus the coefficient of variation of the sitting pulse rate in the present series agrees well with these results quoted.

(2) *Maximum Rate.*—It is surprising that the mean maximum rate in a 5-seconds interval should be as high as 130 per minute in healthy young men performing a very light exercise. The maximum rate would appear to ·be a suitable index for measuring cardiac tolerance, as it is the least variable of the indices chosen, its coefficient of variation being only 9·9 per cent. If the initial heart rate is high the maximum rate reached is also high, the coefficient of correlation being +0·69 with a standard error of 0·116. This does not mean, however, that emotion simply raises the levels of the heart rates evenly throughout the experiment. In fact, where the initial rate is high the increase in the number of beats per minute produced by the exercise is generally low. For example, if the subjects are divided into those with initial rates below and above 85 per minute, the increase with exercise averages 48 beats per minute in the former, and 40 beats per minute in the latter.

This smaller increase is particularly noticeable in those whose resting rate just before exercise shows much increase over the resting rate two minutes earlier; these are presumably the subjects in whom the emotional element is greatest. It would thus appear that during the exercise the emotional increase is lessened and that some factor comes into play to prevent an excessively high maximum rate. Cotton, Rapport, and Lewis (1917) found a similar relationship between the initial and maximum rates recorded after the end of maximal exercise. They explained it on the assumption that " the circulation is capable at a given moment of a certain response to a given effort, and it appears to be a matter of indifference whether this response has been called forth to some extent before the chief stimulation has been applied, providing it has been called forth through similar channels." Boas and Goldschmidt (1932) made similar observations. In the present series, if emotion is considered to play the part of the introductory stimulus before the chief stimulus is applied, the results are in accordance with this theory, although the exercise is very far short of maximal.

(3) *Time of Occurrence of the Maximum Rate.*—It has been generally assumed that the maximum pulse rate reached during exercise occurs at the end. In exercise lasting one minute Peabody and Sturgis (1922) nearly always found the maximum rate during the last 15 seconds. Essex *et al.* (1939), working on dogs, found that in an exercise lasting about 15 minutes the maximum rate for a given amount of work was usually reached within one to three minutes of the beginning of the exercise, and that frequently the pulse rate fell well below the initial rise and remained fairly constant at the lower level. They pointed out that these findings in the dog are in striking contrast with those of previous workers, who found that in man the pulse rate continues to increase throughout the period of exercise until the maximal rate is reached.

The present findings closely resemble those of Essex *et al.* The maximum rate, instead of occurring at the end of the 24 seconds of exercise, is reached on the average 15 seconds after exercise begins. After this maximum the rate falls slightly and continues more or less level till the end. This, which is well shown in Fig. 2, does appear in the records of other workers, though it has
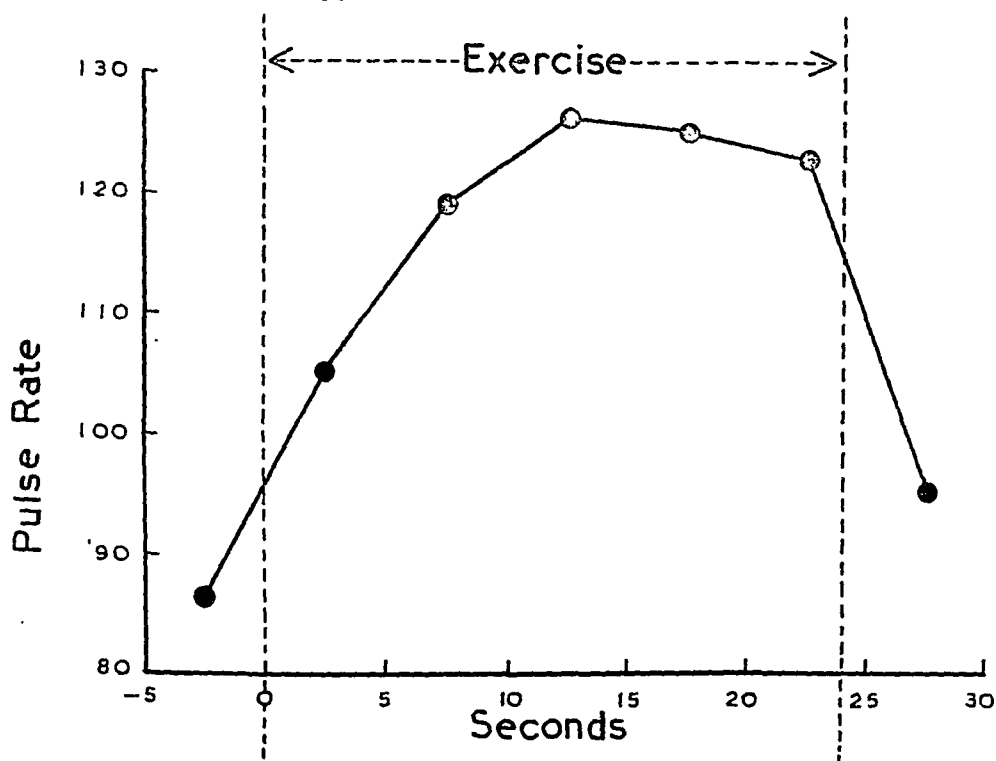
FIG. 2.—The average pulse rates of 75 male students in 5-seconds intervals before, during, and after the standard exercise. The average maximum rate here is slightly lower than that given in the table because the maximum rate does not always fall in the same 5-seconds interval.

not been stressed by them. In experiments on light work (tapping a key) by Bowen (1903) the average curve showed the maximum rate after two and a half minutes in an exercise lasting four minutes. Boas and Goldschmidt (1932) noted that in boys performing exhausting exercise for over three minutes the maximum rate was generally found two minutes after exercise began.

Paterson (1928) found in some cases an early maximum rate followed by a decline before a subsequent slower rise to the level of the early maximum. A curve given by Gillespie, Gibson, and Murray (1925) for light work also showed this effect, and Backwell (1921) (quoted by McDowall, 1939), obtained the same result when the start of the effort was sudden.

It was thought that our early maximum and subsequent slowing during exercise might be because the exercise was started from the sitting posture. Standing up might augment the rate during the first half of the exercise and this might pass off as circulatory adjustments are made. This, however, is not the case, as trials made with exercise starting from the standing posture still show the early maximum rate.

There are two main possibilities concerning the behaviour of the heart when an increased demand is made on the circulation.

The first theory postulates that the amplitude of the heart beat, i.e. its stroke volume or output per beat, is variable ; and thus the reserve capacity of the circulation lies mainly in variations of stroke volume and rate. The second theory postulates that the stroke volume remains nearly constant, and the demands on the circulation during activity are met mainly by variations in rate. A factor of safety is provided during exercise because the tissues are then able to take more oxygen out of a given volume of blood. This theory of the constant output per beat was supported by Henderson (1923 and 1925), while Henderson, Haggard, and Dolley (1927) found that the output per beat remained relatively constant during rest and moderate exertion in ordinary subjects, but that it might be much increased in athletes performing strenuous exercise.

The first theory, that of variable output per beat, was stated by Bainbridge (1919) and was supported by the experiments of Means and Newburgh (1915), and by later work of Lythgoe and Pereira (1925). On this basis, a theory to account for the early maximum rate and subsequent slowing of the heart during the exercise might be put forward as follows. Assuming the frequency and the output per beat to be independently variable, the increase in blood flow required by the exercise might be brought about in the early stages (the first fifteen seconds or so) mainly by increase in the rate, thus giving the rapid rise to the maximum rate. Then, in order to minimize strain on the heart muscle, the output per beat might increase enough to allow a slight slowing off in the rate, the exercise ending before any further increase in rate is needed. The observations of Means and Newburgh on the effects of increasing amounts of work tended to show that the output per beat increased before the frequency.

(4) *Acceleration of the Heart Rate.*—The chief point of interest of this index is that it is a measure of the acceleration of the heart rate, expressed as beats-per-minute per second, and not merely an expression of change of rate. It is, however, very variable, the coefficient of variation being as high as 28·7 per cent. As was pointed out long ago by Bowen (1903), Buchanan (1909), and others, the acceleration begins immediately the exercise starts, and this can clearly be seen on the tracings.

(5) *Number of Extra Beats induced by the Exercise.*—This index is of no great value in the present series of healthy men, but preliminary tests on patients

with heart lesions suggest it may be of interest. There was no significant correlation of extra beats and body weight in the present series.

(6) *Percentage Increase on Initial Rate.*—This has a high coefficient of variation and the variations occur over a wide range, no doubt because the maximum rate remains relatively constant while the initial rate varies widely. Hill, Magee, and Major (1937) found the percentage increase of pulse rate after two maximum pulls on a dynamometer to be very variable, but the absolute rise in rate was about the same in those with slow, medium, or fast resting rates.

(7) *Actual Increase in Beats per Minute caused by the Exercise.*—The relationship of this to the initial rate is dealt with under " maximum rate." The absolute increase in beats per minute here is very variable, in contrast with the results obtained by Hill, Magee, and Major (1937).

(8) *Heart Rate in the 30 Seconds beginning 5 Seconds after Exercise.*—This is highly correlated with the maximum rate, the coefficient being $+0.83$ with a standard error of 0.116. This index, then, which requires no apparatus and can be obtained by palpation, is a fairly reliable guide to the maximum rate reached during the exercise. The regression equation is : maximum rate $=0.72$ post-exercise rate $+ 64$.

Cotton and Dill (1935) using a modified Boas' cardiotachometer recorded the heart rate in four periods of ten seconds each, two immediately preceding and two immediately following the end of exercise. The exercise consisted o walking and running on a flat treadmill and was continued long enough for a steady state to be reached. They concluded that the heart rate during exercise may be predicted from that recorded in the ten seconds following exercise, with an error whose standard deviation is less than 3 per cent ; and that the heart rate fell very little during the first ten seconds after the exercise, and for the next ten seconds only about 6 per cent. The conditions differed from those of the present series in that their exercise was prolonged until a steady state was reached; which, no doubt, accounts for the slow drop after the exercise, in contrast to the rapid drop observed in the present series (see Fig. 2). Gillespie, Gibson, and Murray (1925) stated that while the pulse rate just after exercise was a fairly reliable relative indication of the rate during the exercise, it was impossible to draw inferences therefrom as to the absolute rate.

Paterson (1928) found that the values of the pulse rate during exercise were much higher than one would expect from values taken even immediately after exercise. This is upheld by the present results.

Sinus Arrhythmia

Treadgold (1930) said that sinus arrhythmia was usually of no significance as regards cardiac efficiency unless it was extremely marked. As it is easily detected by the present method of recording, it may be of interest to give its frequency of occurrence. The tracings have been divided into four categories according to the degree of sinus arrhythmia. It was absent in 9 per cent; slight in 29 per cent; marked in 55 per cent; and very marked in 7 per cent.

Thus it will be seen that the condition was present to a marked degree in over 60 per cent of these normal young adults. Fig. 3 shows one such case. In
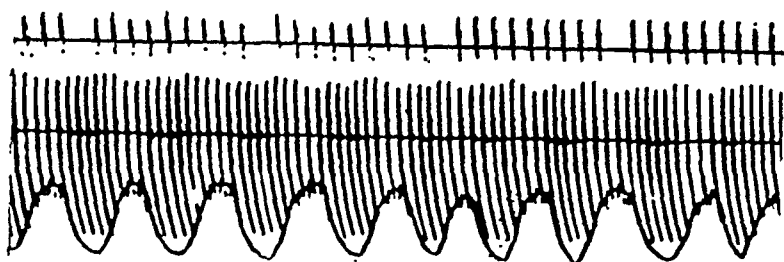
FIG. 3.—This tracing shows marked sinus arrhythmia. Upper tracing, time in seconds. Middle tracing, heart beats. Lower tracing, respiration (the rise of the lever indicates expiration, the fall indicates inspiration).

most cases the sinus arrhythmia disappeared during the exercise, but was especially prominent after it, perhaps due to deeper breathing. Dana (1919) described simple pauses in the heart beat, apparently dropped beats, which occurred in association with simple sinus arrhythmia. About 15 per cent of the present series show this condition in some degree (Fig. 4), but not always
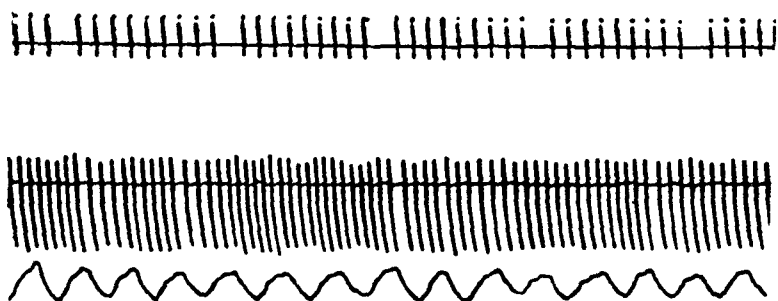
FIG. 4.—This tracing shows simple pauses in the rhythm of the heart. Upper tracing, time in seconds. Middle tracing, heart beats. Lower tracing, respiration.

those with marked sinus arrhythmia. The condition would appear to be some form of sinus block.

It is hoped that this somewhat exhaustive survey of results in a simple cardiac tolerance test will serve as a basis for further tests which are being carried out on the heart rate during exercise in patients with various cardiac esions.

SUMMARY

A simple two-step cardiac tolerance test of very brief duration is described, in which the subject's heart beats are electrically recorded on a smoked drum throughout the test.

From the analysis of the records of 75 healthy male students, the following indices are obtained and discussed: initial rate; maximum rate; time to reach the maximum rate; acceleration of the heart rate; number of extra beats induced by the exercise; actual and percentage increase on initial rate; and the rate after exercise.

The mean values and variability of these indices are given.

I wish to acknowledge my indebtedness to Professor E. P. Cathcart for his interest and encouragement during the progress of the work.

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WILLIAM WITHERING (1741–1799) AND EDGBASTON HALL

BY

K. D. WILKINSON

Edgbaston Hall, once the home of William Withering, and now the club house of the Edgbaston Golf Club, was the venue of the annual dinner of the *Cardiac Society of Great Britain and Ireland* for the Birmingham meeting in May 1939.

The estate is a very old one, and the present house has some close medical associations. The Manor of Edgbaston dates back to the Norman Conquest, when it was valued at thirty shillings a year; and in the reign of King Richard the second, through the marriage of Isabella de Egebaston to Thomas Middlemore, the estate passed to the Middlemores, with whom it remained for more than three hundred years. The Middlemores were an important Roman Catholic family in the Midlands, with very large estates of which the present Duke of Norfolk is co-heir. In 1635, as Roman Catholics, they forfeited their Edgbaston estates, but managed to obtain a forty years lease from the Crown on the payment of one hundred pounds a year. The size of Edgbaston Hall at this time may be judged from the fact that it paid hearth tax on twenty-two hearths.

During the Civil War, the Hall was held for Parliament by the notorious Colonel Fox, who maintained a garrison there for three years. He did so much damage that it was not again inhabited. In 1680, the Hall was dismantled, with the excuse of preventing it acting any longer as a refuge for Papists, and in 1717 the estate was sold to Sir Richard Gough, and shortly afterwards the Hall as it now stands was constructed. An illustration is shown on the next page.

William Withering obtained a fourteen years lease of the Hall and park in January 1786, at an annual rental of two hundred and thirty-seven pounds ten shillings. The lease also states that " he is to replace any sweet carp or tench removed from the pool, is not to dig, plough, break up, or convert into tillage, any part of the estate, under penalty; nor to plant flax seed, rape seed, wood madder, or potatoes, but he is to maintain the wheat crop."

In 1791, Birmingham had most serious riots, fomented by rival religious parties, but based upon political unrest and feelings against Dr. J. Priestley and others who approved the French Revolution. Edgbaston Hall was attacked, but escaped serious damage, being more fortunate than many of the mansions round the city. Withering was neither a non-conformist nor a
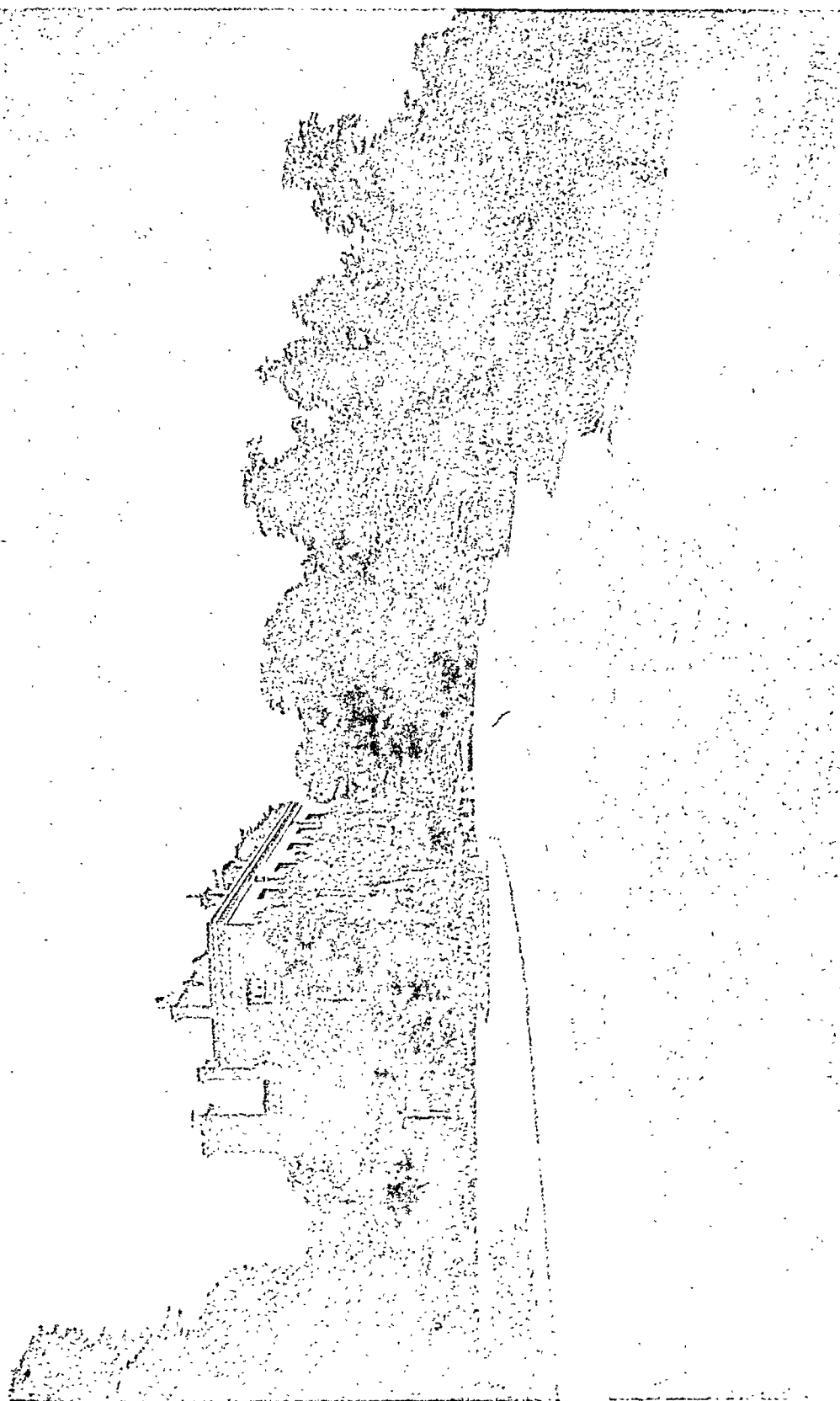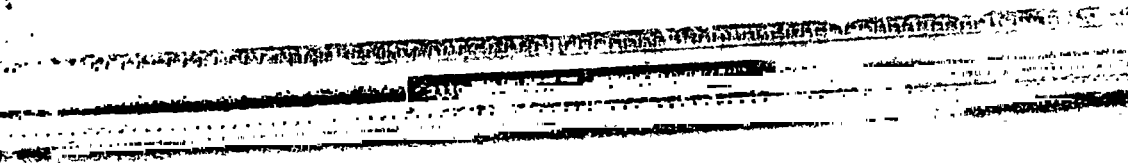
sympathizer with the Revolution, but any house that appeared worth looting was subject to attack, and he was known as a friend of Priestley.

It was at Edgbaston Hall that Withering maintained a botanical garden, and bred cattle and dogs—the cattle breeding was so successful that it paid his rents—and there he met and entertained many of the leading scientists and botanists of his time, for he had a European reputation not only as a physician, but also as a botanist and as a chemist. Shortly before he died in 1799, Withering left the Hall for a milder climate in Sparkbrook, but he only lived at " The Larches " for a week, for he moved on September 28, 1799, and died about 7 p.m. on October 6, aged fifty-eight years and six months.

He was buried in Edgbaston Church on October 10 and there still stands the mural monument with the representations of digitalis and the Witheringia.

In the inscription, he is said to have been born on March 28, 1741, but his son in the memoirs says that he was born on March 17, 1741; probably March 28 was the baptismal date.

To-day in the garden and grounds of the Hall there are still blooms of foxglove—descendants of those plants that Withering himself cultivated—and that surely is the best memorial to his memory.

EXTRACT FROM THE MINUTES OF THE THIRD ANNUAL GENERAL MEETING OF THE CARDIAC SOCIETY, HELD AT BIRMINGHAM ON THURSDAY, MAY 25, 1939. CHAIRMAN: K. D. WILKINSON.

Dinner was held at the Edgbaston Golf Club (Withering's old house), and the Society admired the fine portrait of Withering, lent by the Chairman to look down on the Society from the walls of his old dwelling-house. The original painting, of which this was an excellent copy, was by Carl von Breda and was bought for the Stockholm gallery where it hangs with this inscription :—

> 2339 BREDA, CARL FREDRIK VON,
> svensk, f.1759, d.1818.
> PORTRÄTT AU DEN ENGELSKE LAKAREN
> WILLIAM WITHERING.   sign. 1792.

[A photograph of this is shown on the previous page.]

John Hay, in his usual felicitous manner, proposed the health of the Society, coupled with the name of the Chairman. The Chairman (Wilkinson) replied with a charming sketch of some aspects of Withering's life and work, and proposed the health of the Secretary. The Secretary replied shortly.

John Parkinson

9th May, 1940

ERRATA

Page 101, line 15 : *for* 0·5 mV. *read* 0·05 mV.

Page 105, Summary, line 2 : *for* 0·5 mV. *read* 0·05 mV.

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